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ACUTE EPIDEMIC MYALGIA OR PLEURODYNIA

CLINICAL COURSE AND DIAGNOSIS OF THE DISEASE IN CHILDREN

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SAN FRANCISCO

Although epidemic pleurodynia is not uncommon in childhood, most of the contributions on this subject have been concerned primarily with its manifestations during the years of early adult life.

During the epidemic in Boston in 1933 an opportunity arose to study nineteen cases of this disease in children under 8 years of age.[1] While it was known that acute epidemic myalgia was prevalent at that time, a number of the earlier cases in this group were at first unrecognized, because of failure to appreciate that the clinical course of the condition in young children often presents certain radical departures from the picture usually described for adults. My purpose in this report is to direct attention toward the symptomatology of the disease in children and to point out some of the more important variations between the infection in childhood and that in adult life.

HISTORY

Acute epidemic myalgia has been variously referred to as the Bornholm disease, diaphragmatic pleurodynia, the Bamle disease, epidemic myositis, "devil's grip," the Sylvest-Bings disease, epidemic pleurodynia and epidemic diaphragmatic spasm.

The disease was first observed in Iceland in 1856, and shortly thereafter it appeared in Norway.[2] Since then cases have been described in several countries, including Finland, Denmark, Sweden, the United States, Germany, Portugal and England.[3] It is prevalent throughout the Scandinavian peninsula and is occurring with increasing frequency in this country, where six epidemics have been reported in the past

1. Studied at the Infants' and Children's Hospitals, Boston.

2. Epidemic Myalgia, or Pleurodynia, editorial, J. A. M. A. **102**:460 (Feb. 10) 1934.

3. (*a*) Jorge, R.: Sur la myalgie épidémique du tronc (maladie de Bornholm) dans Lisbon, Bull. Office internat. d'hyg. pub. **25**:65 (Jan.) 1933. (*b*) Sylvest, E.: La maladie de Bornholm (myositis acuta epidemica), ibid. **24**:1431 (Sept.) 1932. (*c*) Petrén, E.: Outbreak of Epidemic Myalgia in Sweden in 1931, Svenska läk.-tidning **30**:1153 (Nov. 3) 1933. (*d*) Heckscher, H.: Myositis Epidemica-Serositis, Acta med. Scandinav. **80**:251, 1933. (*e*) Pickles, W. N.: "Bornholm" Disease, Account of Yorkshire Outbreak, Brit. M. J. **2**:817 (Nov. 4) 1933.

decade.[4] The first outbreak in the United States took place in and around Charlottesville, Va., in 1888.[5] The last appeared in Boston during the summer and early fall months of 1933.[6] The disease has been found only in the southern and eastern states.

ETIOLOGY

Epidemic myalgia is moderately infectious, and it is not unusual for several members of the same family to be afflicted. The causative agent and mode of transfer remain obscure although it seems likely that entry is via the nasopharynx, with a droplet infection as the most important factor. In 1924 Small[7] reported that he found within the erythrocytes of patients suffering from the disease a protozoan organism which he designated Plasmodium pleurodyniae. Subsequent investigators have not been able to corroborate this work. Crone and Chapman failed to transmit the disease by intravenous injection of whole blood from a patient to a normal person.[6a] No immunity is conferred by a single attack.

The period of incubation has not been definitely established. Pickles recently described several cases that developed in an English family. He observed that symptoms appeared at intervals of four days [3e] and concluded that the period of incubation was short. In contradistinction, Crone and Chapman noted an instance in which two weeks elapsed between the appearance of symptoms in a brother and their development in a sister. The time of exposure was definitely ascertained in three of the cases included in the present report, and in each one there was a lapse of from ten to twelve days before the occurrence of initial manifestations. Thus the burden of evidence, though meager, points to an incubation period of from ten to fourteen days.

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4. Payne, G. C., and Armstrong, C.: Epidemic Transient Diaphragmatic Spasm: A Disease of Unknown Etiology, Epidemic in Virginia, J. A. M. A. **81**:746 (Sept. 1) 1923. Greene, D.: Epidemic Pleurodynia, Arch. Pediat. **41**:322 (May) 1924. Hanger, F. M., Jr., et al.: An Epidemic of Mild Fever of Unknown Nature, J. A. M. A. **81**:826 (Sept. 8) 1923. Wood, R. B.: An Epidemic of Acute Pleurodynia in Tennessee, J. Tennessee M. A. **18**:255 (Jan.) 1926. Torrey, R. G.: Epidemic Diaphragmatic Pleurodynia or "Devil's Grip," Am. J. M. Sc. **168**:564 (Oct.) 1924. Churchill, F. S., et al.: An Epidemic of Undetermined Nature: Dengue? J. A. M. A. **87**:821 (Sept. 11) 1926.

5. Dabney, W. C.: Account of an Epidemic Resembling Dengue, Which Occurred in and Around Charlottesville and the University of Virginia in June 1888, Am. J. M. Sc. **96**:488, 1888.

6. (*a*) Crone, N. L., and Chapman, E. M.: Epidemic Pleurodynia, New England J. Med. **209**:1007 (Nov. 16) 1933. (*b*) Richter, A. B., and Levine, H. D.: Epidemic Pleurodynia, J. A. M. A. **102**:898 (March 24) 1934.

7. Small, J. C.: A Protozoan Organism Within the Erythrocytes of Patients Suffering from Epidemic Pleurodynia ("Devil's Grip"), Am. J. M. Sc. **168**:570, 1924.

The disease is distinctly seasonal and reaches epidemic proportions during the summer and fall months, although sporadic cases probably exist throughout the year and are not recognized. Although no age group is exempt, the condition is uncommon in persons over 25 or 30 years of age and is limited largely to young adults and children. There is no sexual predilection.

GENERAL CHARACTERISTICS

As described in adults epidemic pleurodynia is characterized by an abrupt onset with excruciating pain, usually of thoracic, and occasionally of epigastric, origin. It is exacerbated by cough, movement or deep inspiration; tenderness is frequently present. The temperature ranges from 101 to 104 F., and there are usually anorexia, prostration of some degree and headache. Nausea and vomiting are not uncommon, and pains in the back and extremities may occur. On examination there is a significant absence of pertinent physical findings in the chest, although in cases in which abdominal discomfort is severe considerable rigidity of the rectus muscles is often present. The leukocyte count is either normal or moderately increased. The average duration is from forty-eight to seventy-two hours, complications are rare, and recovery has been invariable. A recurrent type is sometimes seen in which one or more exacerbations of relatively mild character occur every few days. Cases of this type occasionally persist for three weeks or longer.

CLINICAL COURSE IN CHILDREN

This brief clinical consideration of acute epidemic myalgia in children is based on a review of nineteen cases in which the children ranged in age from 5 months to 8 years.[8]

The disease usually occurred in a person apparently in excellent health, being ushered in abruptly by severe pain, general malaise and fever. In a few instances there was evidence of preceding infection of the upper respiratory tract. Pain was invariably the outstanding symptom, and its distribution was particularly worthy of note. Unlike that most often described in adults, the pain was localized in the abdomen rather than in the thorax. Only three patients had pain limited entirely to the region of the thorax. Five patients had both abdominal and thoracic discomfort, and the other eleven had abdominal pain only. This was severe and paroxysmal in nature, usually inclined to be diffuse or vaguely localized in the midepigastrium and at times aggravated by movement. Anorexia was extreme; nausea and vomiting occasionally obtained. In some of the older children chills were common. An out-

8. The upper age limit for admission to the hospital is 12 years.

standing symptom presented by many was profuse perspiration. Hyperhidrosis has been described in adults but is apparently of rather unusual occurrence.

The chest of each patient was normal. Abdominal manipulation usually elicited voluntary spasm and superficial tenderness similar to those often encountered in pneumonia. There was no true rigidity or marked tenderness. Rectal examinations revealed no pertinent findings. The temperature recorded rectally varied from 102 to 103.5 F. and averaged 102.5 F. The leukocytes numbered from 9,000 to 17,110, with an average of 12,900; there was neutrophilia, the count averaging 75.6 per cent. No protozoan organisms were found within the erythrocytes. The usual duration of the disease was four days, with extremes of one and seven days.

The recurrent type of infection is apparently much commoner in children, for in this series 75 per cent had a return of their febrile paroxysm, usually on the third, and occasionally on the fourth, day of illness. This recurrence appeared after an asymptomatic period of from twenty-four to seventy-two hours and was not unlike the "dromedary phenomenon" of poliomyelitis. Three patients had two secondary paroxysms, and one child had three. The temperature was not as high as in the initial attack, and pain was rarely extreme. In the cases mentioned by Pickles [3e] all the children had a return of symptoms on the third day.

The following cases illustrate acute epidemic myalgia as it appears in the young child.

REPORT OF CASES

CASE 1.—F. S., a boy of 16 months, was admitted to the Infants' Hospital on Sept. 21, 1933, because of fever and grunting respirations for twelve hours. The child had previously been well. There had been no evidence of infection of the respiratory tract. A brother, 5 months of age, had been in the hospital ten days before with a similar ailment. Examination of F. S. disclosed a well developed and well nourished baby bathed in perspiration and appearing acutely ill, with flushed skin, rapid grunting respirations and dilated alae nasi. When disturbed, the infant shrieked as though in severe pain. There were a slight mucoid nasal discharge, moderate pharyngeal injection and some tonsillar hypertrophy. The chest was normal. The abdomen was held tense by a voluntary contraction that could easily be relaxed; there was some diffuse tenderness. The rectum was normal. Other findings included fever, the temperature being 103 F., marked acetonuria and a leukocyte count of 12,800 with 82 per cent granulocytes. Culture of the blood, Wassermann and Mantoux tests and roentgenographic examination of the chest gave negative results. Repeated examination of the blood failed to show any intracellular sporozoa. On the day after entry the infant appeared bright and happy and was afebrile. The subsequent course was uneventful.

CASE 2.—M. C., a girl 5 years of age, was brought into the Children's Hospital on Aug. 1, 1933, with severe abdominal pain. Three days before, while the child was apparently well, anorexia and pain in the right upper quadrant of the abdomen developed, followed by vomiting. During the night there were several attacks

of severe pain accompanied by profuse perspiration. On the following morning the child had apparently recovered, and for the next twenty-four hours was active and playful. However, paroxysmal, diffuse abdominal pain then returned and was accompanied by fever and drowsiness. Headache became severe. After these symptoms continued for ten hours, the child was taken to the hospital. Examination showed a well developed and well nourished girl who appeared acutely ill and drowsy. The respiratory rate was slightly increased, and there was questionable rigidity of the neck. Moderate pharyngeal and tonsillar inflammation was present. The lungs were clear. Examination of the heart showed a soft systolic murmur at the apex. The abdomen was soft throughout with no tenderness. Neurologic examination disclosed nothing remarkable. The temperature was 102 F. The leukocytes numbered 9,700 with 92 per cent polymorphonuclears. The urine contained large amounts of acetone. Roentgenograms of the chest and the abdomen showed a normal condition. The Wassermann, Hinton and Mantoux reactions were negative. Poliomyelitis was epidemic at that time, and because of the questionable rigidity of the neck lumbar puncture was performed. The spinal fluid was normal. Twelve hours after admission the temperature had become normal, and it remained so until the third day, when it rose to 102 F. At that time abdominal pain again developed. Physical examination revealed nothing significant. The symptoms continued for twelve hours during this recurrence, after which convalescence was uninterrupted. No intracellular sporozoa were found in the blood.

DIAGNOSIS AND TREATMENT

It should be kept in mind that these cases are cited as typical examples of epidemic pleurodynia. In many cases the course is vague. Unless the disease has assumed epidemic proportions diagnosis is extremely difficult. In adults the condition is said to simulate pleurisy, appendicitis, pericarditis, influenza, dengue, herpes zoster and angina pectoris. Among children it is to be differentiated from early pneumonia, pyelitis, mesenteric adenitis, appendicitis and poliomyelitis. In small infants the rapid, shallow respirations, dilatation of the alae nasi and expiratory grunt strongly suggest early pneumonitis; in older children the picture often resembles that of acute appendicitis or mesenteric adenitis. In localities where dengue occurs this disease must also be considered.

In the past, acute epidemic myalgia has been treated symptomatically and rather unsuccessfully. The therapeutic measures employed have had little effect on the course or on the duration of the disease. It has been particularly difficult to obtain any marked degree of relief from the severe pain. When the localization is largely pleural, strapping of the chest, application of dry heat and the oral administration of codeine have been of some value. As the condition is infectious, isolation should be observed.

If a plasmodium is of etiologic significance in this condition, as Small postulated, quinine or one of its derivatives should theoretically be the therapeutic agent of choice. Therefore, quinine sulphate was given orally in moderate amounts to two patients suffering from recur-

rent myalgia who had not responded to previous therapy. These patients were members of my family. In one, severe paroxysms had occurred every few days for over two weeks; in the other, symptoms had been present for eight days. In both patients after quinine sulphate had been administered for twelve hours there was a complete cessation of pain and the temperature dropped to a normal level. It should be of interest in the future to give this drug a proper therapeutic and perhaps a prophylactic trial in cases of epidemic pleurodynia.

SUMMARY

Nineteen cases of acute epidemic myalgia in young children are reviewed. Attention is directed toward certain features of the disease that are peculiar to childhood and that have escaped previous emphasis. Thoracic pain is the predominant symptom of infection in adults, while in children there is a marked tendency toward abdominal pain, with little or no thoracic involvement. Children are also frequently afflicted with a recurrent type of the disease in which one or more febrile paroxysms occur following asymptomatic periods of from two to three days. Familiarity with the clinical course of the condition in children should considerably facilitate early diagnosis, although the recognition of sporadic cases is extremely difficult.

It is suggested that quinine may be of considerable prophylactic and therapeutic value in the management of acute epidemic myalgia or pleurodynia. The results in two cases are described.

DIGESTION OF MILK AND OF MODIFIED MILK IN VITRO

DOROTHY FETTER, PH.D.
AND
FREDERIC W. SCHLUTZ, M.D.
CHICAGO

These experiments were carried out in order to note the comparative speeds of digestion of the usual modifications of milk used in the feeding of infants at varying p_H concentrations and also to note the effect of adding rennin [1] to the various foods. Emphasis has been placed on the relation of the p_H of the gastric contents to digestion. This disadvantage of feeding cow's milk to babies has been in part ascribed to its high buffer effect in neutralizing gastric juice, and, conversely, the greater digestibility of human milk has been laid to the fact that it does not neutralize gastric juice to such an extent. The preparations of acid milk used in the feeding of infants lower the p_H of the gastric contents and so are said to favor digestion, stimulate gastric motility and increase the antiseptic properties of the gastric juice.

METHOD

The milk products studied were untreated cow's milk, Carnation milk, buttermilk, Mead's powdered milk, Mead's protein milk and Mead's lactic acid milk. The milk product was so prepared that 100 cc. of it contained approximately 4 Gm. of protein. Fifty cubic centimeters of the milk product was added to 50 cc. of an artificial gastric juice composed of 0.5 per cent hydrochloric acid and 1 Gm. of pepsin. Half of the mixture was set aside, and to the other half 8.5 Gm. of vanilla flavored Junket was added. The p_H of the mixture was adjusted to the desirable value by means of the addition of sodium hydroxide or sodium carbonate. The bottles containing the mixture were placed in a rotating machine in an incubator set at 37 C. in order that digestion could go on under conditions somewhat approaching those of the stomach. Before they were placed in the incubator, samples were taken from them in order to test for the soluble nitrogen which might be present. Thereafter the bottles were withdrawn from the incubator every two hours for a period of eight hours, and samples of the contents were analyzed for soluble nitrogen. As digestion progresses the proteins are broken down, and the rise in soluble nitrogen is taken to be indicative of the progress of digestion.

The quantity of soluble nitrogen was determined in two ways. The first was the Sorenson method of titration for amino-acids with formaldehyde.[2] This method

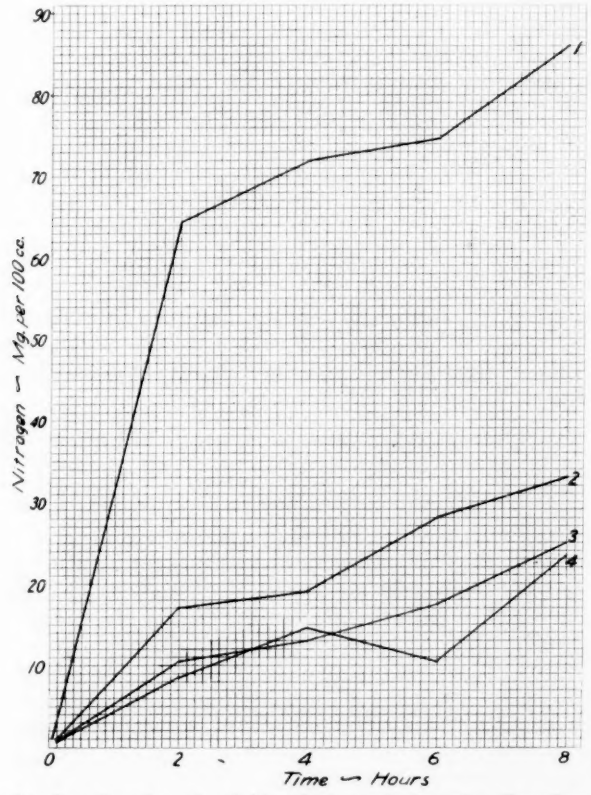
From the Department of Pediatrics of the University of Chicago.

1. Junket, as prepared by the Christian Hansen Company of Little Falls, N. Y., was used as a source of rennin.

2. Henriques and Sorenson: Ztschr. f. physiol. Chem. **64**:120, 1907.

shows the total amount of acids present. Therefore, we titrated a similar sample of the milk mixture without adding formaldehyde in order to find the amount of acids which were not amino-acids. The quantity of soluble nitrogen present in the amino-acids can be calculated after the total amount of amino-acids is subtracted from the total amount of soluble nitrogen.

The second method used for the determination of the soluble nitrogen content was as follows: The sample taken was diluted with an equal volume of water and filtered according to the method of Hess, Koch and Sennewald.[3] A quantita-



Curves showing the rise of soluble nitrogen during the digestion of untreated cow's milk, as determined by the micro-Kjeldahl method of Koch and McMeekin. The number *1* represents milk plus Junket (p_H 4.5); *2*, milk (p_H 4.5); *3*, milk plus Junket (p_H 3), and *4*, milk (p_H 3).

tive determination of nitrogen in these filtrates was then made by the direct nesslerization micro-Kjeldahl method of Koch and McMeekin.[4]

Fifteen experiments for each type of milk mixture at each p_H studied were made. Our results are incorporated in the accompanying table and in the chart, which shows the average figure for all fifteen experiments.

3. Hess, J. H.; Koch, E. M., and Sennewald, Z. C.: Peptic Digestion of Cow's Milk, J. A. M. A. **87:**1360 (Oct. 23) 1926.

4. Koch, F. C., and McMeekin, T. L.: J. Am. Chem. Soc. **46:**2066, 1924.

*Average Rise in Soluble Nitrogen Content as Shown in Fifteen Experiments**

Type of Milk and Method	2 Hours	4 Hours	6 Hours	8 Hours	p_H
Milk					
Sorenson	7.77	5.48	8.16	9.68	2.0
Sorenson	7.07	8.28	10.79	15.75	3.5
Sorenson	1.12	4.66	2.61	4.34	4.5
Koch and McMeekin	8.90	14.70	10.60	23.50	3.5
Koch and McMeekin	17.00	19.20	28.00	32.90	4.5
Milk and Junket					
Sorenson	8.25	9.85	9.77	14.30	2.0
Soresson	6.26	8.23	8.90	12.77	3.0
Sorenson	20.17	24.50	23.66	24.88	4.5
Koch and McMeekin	10.90	13.10	17.60	25.80	3.0
Koch and McMeekin	64.10	72.00	74.50	86.80	4.5
Evaporated milk					
Sorenson	7.48	9.58	8.41	14.37	2.2
Sorenson	10.18	8.34	11.75	15.51	3.2
Sorenson	0.84	2.10	3.38	6.30	4.5
Koch and McMeekin	15.50	26.50	25.70	30.00	3.2
Koch and McMeekin	21.70	17.60	33.30	39.70	4.5
Evaporated milk and Junket					
Sorenson	13.38	14.86	12.29	17.36	2.0
Sorenson	11.20	11.34	13.82	15.24	3.0
Sorenson	16.33	16.52	19.46	21.28	4.5
Koch and McMeekin	17.70	27.90	22.90	37.10	3.0
Koch and McMeekin	46.20	51.50	57.10	70.20	4.5
Powdered milk					
Sorenson	11.92	13.57	16.51	16.54	2.3
Sorenson	8.53	9.24	12.18	13.19	4.2
Koch and McMeekin	18.50	19.70	17.10	30.50	4.2
Koch and McMeekin	13.80	25.20	18.70	27.40	2.3
Powdered milk and Junket					
Sorenson	21.55	21.46	24.45	26.65	2.2
Sorenson	18.80	22.44	22.18	25.28	4.3
Koch and McMeekin	36.00	38.80	32.20	39.10	4.3
Buttermilk					
Sorenson	9.12	11.25	12.61	13.59	2.4
Sorenson	7.29	9.66	12.54	14.93	3.0
Sorenson	No digestion				
Koch and McMeekin	18.60	18.20	22.70	32.70	2.4
Koch and McMeekin	15.30	16.60	17.60	25.90	3.0
Koch and McMeekin	16.70	20.80	19.00	26.80	4.5
Buttermilk and Junket					
Sorenson	10.80	11.49	13.16	16.31	2.3
Sorenson	6.38	8.73	12.57	15.18	3.0
Sorenson	20.55	22.95	14.59	21.14	4.5
Koch and McMeekin	16.70	16.60	13.10	17.50	2.3
Koch and McMeekin	11.60	11.40	13.10	18.20	3.0
Koch and McMeekin	28.00	32.00	29.90	41.60	4.5
Protein milk					
Sorenson	9.11	.....	16.14	20.53	1.8
Sorenson	10.68	10.30	12.63	15.04	3.0
Sorenson	1.68	4.00	5.08	6.98	4.5
Koch and McMeekin	33.50	37.50	50.00	61.90	3.0
Koch and McMeekin	25.40	29.80	30.80	36.90	4.5
Protein milk and Junket					
Sorenson	11.95	12.05	14.10	15.29	1.8
Sorenson	8.51	10.68	12.18	13.28	3.0
Sorenson	10.78	10.24	13.72	12.18	4.5
Koch and McMeekin	36.52	44.20	49.70	62.70	3.0
Koch and McMeekin	35.90	40.80	40.00	45.50	4.5
Lactic acid milk					
Sorenson	9.08	11.34	13.68	16.41	1.7
Sorenson	8.12	10.67	13.84	16.37	3.0
Sorenson	No digestion				4.5
Koch and McMeekin	14.80	17.10	20.60	29.10	3.0
Koch and McMeekin	No digestion				
Lactic acid milk and Junket					
Sorenson	8.48	10.75	12.97	15.46	1.7
Sorenson	7.31	10.62	12.68	15.31	3.0
Sorenson	12.69	17.19	17.76	16.02	4.5
Koch and McMeekin	14.00	14.10	14.10	16.10	3.0
Koch and McMeekin	36.30	46.30	36.30	58.20	...

* The rise of soluble nitrogen is expressed in milligrams of nitrogen per hundred cubic centimeters.

RESULTS

Consideration of the table and the graph shows that artificial gastric juice composed of 50 cc. of 0.5 per cent hydrochloric acid plus 1 Gm. of pepsin digests milk and modified milk at a p_H of from 1.8 to 3, as shown by the rise in the soluble nitrogen content of a mixture of 50 cc. of milk and 50 cc. of gastric juice. From one third to one half of the total digestion was accomplished in the first two hours, and the remaining digestion was accomplished more gradually over the last six. The total rise in soluble nitrogen was from 15 to 20 mg. of nitrogen per hundred cubic centimeters according to one method of determination (Sorenson's method of titration with formaldehyde) and from 20 to 40 mg. of nitrogen per hundred cubic centimeters according to another method (Koch and Meekin's modification of the micro-Kjeldahl method). The addition of rennin to the mixture of milk and gastric juice caused no rise in the soluble nitrogen content when added to acid milks and very little rise when added to nonacid milks.

At a p_H between 4 and 5 very little or no digestion of milk or modified milk took place when the food was mixed with artificial gastric juice without rennin. When rennin was added, however, digestion was speeded up so that the first two thirds or three fourths of the total digestion occurred in two hours. The total digestion showed a rise of from 20 to 25 mg. of nitrogen per hundred cubic centimeters by the Koch and McMeekin modification of the micro-Kjeldahl method.

According to our experiment, then, digestion of cow's milk is the most speedy and complete at a p_H between 4 and 5 in the presence of rennin and pepsin. This is true also for all other types of milk except Mead's protein milk.

A study of the table reveals that these different milks showed little difference in speed of digestion at the same p_H. However, the untreated cow's milk showed a somewhat slower digestion during the first two hours than the other milks, and evaporated milk came nearest to it. Powdered milk and the acid milks showed a somewhat greater increase in soluble nitrogen during the first two hours.

COMMENT

The optimum p_H for digestion is reported as being between 2 and 3. This varies according to the type of protein fed and the presence of various salts. We found that digestive activity goes on within this range of hydrogen ion concentration for the protein of milk regardless of whether rennin is present. At higher p_H concentrations rennin is necessary, and digestion is more speedy and complete. Hess, Koch and Sennenwald [3] found that at a p_H above 5 digestion is slower than at lower hydrogen ion concentrations. At a p_H of 4.7 they reported favorable digestion. They used rennin in all their digestive mixtures.

The data presented can be interpreted as indicative of the action of rennin in the digestion of milk and of the action of this enzyme at different degrees of acidity.

Whether rennin exists as a separate entity apart from pepsin has been questioned. Pavlov called attention to the fact that a clotting action occurs with all proteolytic enzymes. He showed that the clotting time of milk in the stomach of adult dogs varies directly with the digestive activity, and so he reasoned that the time effects may be the results of the same enzyme.

Hammarsten and Schmidt-Nielson, however, prepared solutions which have a rennin but not a peptic action, and vice versa. They found that the addition of acid greatly accelerates the activity of pepsin but has not this effect on rennin. Tauber and Kleiner [5] produced an extremely active preparation of rennin free from peptic activity from the fourth stomach of the calf by fractional iso-electric precipitation. Van Dam [6] stated that the coagulation time of milk is inversely proportional to the hydrogen ion concentration. Since rennin acts in a neutral solution while pepsin requires acidity for its activity, it may be assumed that rennin is responsible for this coagulation.

The action of rennin is thought to be either the splitting of the molecule of casein into a peptone-like body plus a molecule of soluble paracasein [7] or the splitting of a molecule of casein into two molecules of paracasein.[8] The paracasein combines with calcium to form an insoluble curd (calcium casein). Van Slyke [9] showed that casein and paracasein are chemically indistinguishable by elementary analysis, by amino-acid distribution or by racemization. The outstanding chemical difference between them, which has a bearing on their colloidal property of primary gels, is indicated by the observation of Van Slyke and Bosworth [9] that paracasein combines with twice as much base as casein for the lower concentration of alkali. Hoffman and Gortner [10] showed that the chemical binding of acids and alkalis by proteins occurs between p_H 2.5 and 10.5. The clotting of rennet occurs in this range according to Palmer and Richardson.[11]

Our experiments show that rennin, as found in Junket, has its greatest effect at a p_H of between 4 and 5. At this p_H range there is little

5. Tauber and Kleiner: J. Biol. Chem. **96**:475, 1932.

6. van Dam, W.: Ztschr. f. physiol. Chem. **58**:295, 1908.

7. Porcher: Chimie et industrie **19**:569 and 809, 1928.

8. Bosworth, A. W.: Studies of Infant Feeding, Am. J. Dis. Child. **22**:193 (July) 1921.

9. Van Slyke, L. L., and Bosworth, A. W.: J. Biol. Chem. **14**:203, 1914.

10. Hoffman, W. F., and Gortner, R. A.: Colloid Symposium, Monogr. 2, New York, The Chemical Catalog Company, Inc., 1925, p. 209.

11. Palmer, L. S., and Richardson, G. A.: Colloid Symposium, Monogr. 3, New York, The Chemical Catalog Company, Inc., 1925, p. 112.

breakdown of the proteins of the milk products when pepsin is the only enzyme used in the gastric juice. At lower p_H values, the effect of rennin is slight, and digestion goes on with pepsin with or without the action of rennin. Our experiments, then, indicate that rennin is a separate entity from pepsin, active at a different p_H.

All the milk preparations which we have used form smaller curds than untreated milk. However, the action of rennin is to form paracasein from casein, and the coagulation of milk (often considered due to rennin) depends on the condition of the calcium salts and on the concentration and the acidity of the solution. This primary formation of paracasein may facilitate the further breakdown of proteins regardless of the formation of clots, and therefore the addition of rennin to these modified milks is a chemical rather than a physical help.

DIGESTION OF MILK AND OF MODIFIED MILK IN VIVO

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Work which we previously carried out in vitro [1] showed that under all conditions which we studied cow's milk and certain modifications of it were digested with greatest speed and completeness at a p_H of 4.5 when rennin [2] was present in the artificial gastric juice.

The milks which we studied were untreated cow's milk, Carnation milk, Mead's powdered milk, Mead's lactic acid milk, Mead's protein milk and buttermilk. We also studied the effect of adding rennin to cow's milk, Carnation milk and powdered milk. Since in our experiment in vitro we found that the addition of rennin to acid milks did not increase the speed of digestion as much as its addition to nonacid milks, we did not add rennin to the acid milks studied in vivo.

We wished to see how the digestion of the milk mixtures which we had studied in vitro compared with the digestion in the human stomach. We also wished to note whether the addition of rennin has the same influence when added to the milk in normal gastric juice as when added to that in artificial gastric juice. A third object of our present study was to see whether the speed of digestion of these milks in the human stomach could be correlated with the emptying time of the stomach after ingestion of these same foods. Formerly we had studied the effect of untreated whole milk and of modified milk on the emptying time of the stomach, as shown by the onset of gastric hunger contractions after feeding these preparations.[3]

Since the breakdown of protein results in soluble products containing nitrogen, we followed the progress of digestion of the milks by determination of the soluble nitrogen in the gastric contents of five children after their ingestion of the different foods. The children ranged in age from 7 to 14. All of them were suffering from congenital

From the Department of Pediatrics, University of Chicago.

1. Fetter, D., and Schlutz, F. W.: Digestion of Milk and of Modified Milk in Vitro, Am. J. Dis. Child., this issue, page 2.

2. Junket, as prepared by the Christian Hansen Company of Little Falls, N. Y., was used as a source of rennin.

3. Schlutz, F. W., and Fetter, D.: Effect of Milk and Modified Milk on Gastric Contractions, Am. J. Dis. Child. **45**:480 (March) 1933.

deformities requiring orthopedic attention. The gastro-intestinal tract was considered normal in all instances.

Our subjects were fed 200 cc. of the milk to be studied. In order to study the effect of rennin, we added to this 34 Gm. of Junket. Each child was tested twice for every kind of milk studied. At ten minute intervals and every half hour after ingestion of milk preparations, samples of the gastric contents were withdrawn. These samples were filtered, and the clear filtrate was tested for the soluble nitrogen content.[4] The p_H of the material was also taken. The method used for the determination of the soluble nitrogen was the direct nesslerization micro-Kjeldahl method of Koch and McMeekin.[5]

For all subjects we studied the soluble nitrogen content of the gastric juice secreted after the injection of 0.005 Gm. of histamine per kilogram of body weight. By this means the nitrogen which did not originate in the protein of milk could be estimated. We found this quantity to be low in all cases (from 26 to 36 mg. of soluble nitrogen per hundred cubic centimeters).

In order to see whether the source of rennin itself contained any nitrogen which could be broken down and so influence the results, we determined the soluble nitrogen in the gastric contents after ingestion of 34 Gm. of Junket dissolved in 200 cc. of water. The resulting gastric contents contained so little nitrogen that in samples withdrawn at intervals during a one and one-half hour period the quantity could not be determined by our method. The soluble nitrogen content was lower than that of pure gastric juice, undoubtedly because of its dilution. We could assume, then, that no breakdown of the Junket itself influenced the rise in soluble nitrogen obtained when this source of rennin was added to our milk mixtures.

These studies on the gastric contents of the human subject have obvious disadvantages in that the quantity and quality of the secreted gastric juice cannot be controlled and that during digestion some of the material is constantly being lost from the stomach. We can merely assume that the quantity of soluble nitrogen in the samples of the gastric contents which we withdrew represents the progress of digestion. Our results prove consistent in regard to the time at which the rise and fall of soluble nitrogen occurred in each child. While there was a variation of the actual quantity of soluble nitrogen found in the two studies on the same milk in the same subject, the variation was not as great as might be expected, since the secretion of gastric juice was not controlled. We noted that in the case of the more slowly digested milks the reading

4. Hess, J.; Koch, E., and Sennewald, Z.: Peptic Digestion of Cow's Milk, J. A. M. A. **87**:1360 (Oct. 22) 1926.

5. Koch, F. C., and McMeekin, T. L.: J. Am. Chem. Soc. **46**:2066, 1924.

taken one-half hour after ingestion showed a smaller quantity of soluble nitrogen that that taken ten minutes after ingestion. This may have been due to dilution of the milk by the increasing quantity of gastric juice. Subsequently a rise in the amount of soluble nitrogen occurred.

TABLE 1.—*Changes in the p_H and in the Quantity of Soluble Nitrogen of the Gastric Contents of One Child* *

Kind of Milk	Time After Ingestion	p_H	Nitrogen, Mg. per 100 Cc.	Increase, Percentage
Untreated cow's milk	10 minutes	...	83.6	....
	½ hour	...	58.3	—17
	1 hour	...	69.9	—16
	1½ hours	...	101.0	+20
	2 hours	...	86.5	+ 3
	2½ hours	...	52.6	—37
Milk and Junket	10 minutes	4.2	64.5	....
	½ hour	4.2	80.3	+24
	1 hour	3.3	76.9	+19
	1½ hours	2.1	79.6	+23
	2 hours	1.8	81.9	+26
	2½ hours	1.8	75.5	+17
Powdered milk and Junket	10 minutes	5.2	68.9	....
	½ hour	4.9	98.0	+42
	1 hour	2.6	121.2	+75
	1½ hours	1.9	43.4	—22
	2 hours	1.9	35.0	—49
Lactic acid milk	10 minutes	3.9	103.0	....
	½ hour	3.7	105.2	+ 2
	1 hour	...	63.4	—37
	1½ hours	2.1	93.0	— 9
Protein milk	10 minutes	4.5	168.0	....
	½ hour	4.0	183.4	+ 9
	1 hour	2.7	155.0	— 7
	1½ hours	...	153.8	— 7
	2 hours	1.5	69.2	—52
Evaporated milk	10 minutes	4.2	125.8	....
	½ hour	3.3	134.2	+18
	1 hour	2.1	100.5	—10
	1½ hours	1.6	54.3	—51
	2 hours	1.3	36.3	—68
Evaporated milk and Junket	10 minutes	4.3	98.0	....
	½ hour	3.8	117.6	+20
	1 hour	2.3	80.0	—18
	1½ hours	1.6	46.5	—52
	2 hours	2.9	38.6	—60
Powdered milk	10 minutes	4.0	109.3	....
	½ hour	3.3	62.6	—42
	1 hour	2.1	108.1	— 1
	1½ hours	2.0	97.5	—10
Buttermilk	10 minutes	4.0	114.2	....
	½ hour	3.5	118.3	+ 3
	1 hour	1.6	64.9	—43
	1½ hours	1.6	36.2	—68

* The soluble nitrogen content of the gastric juice secreted after the injection of 0.005 Gm. of histamine per kilogram of body weight was 26 mg. per hundred cubic centimeters.

These results can be studied in the accompanying tables. Table 1 shows the complete set of results obtained for one subject. Table 2 shows the time at which the quantity of soluble nitrogen was greatest for all five subjects.

Table 1 shows the soluble nitrogen content in the samples of gastric contents which we withdrew. The changes in the quantity of soluble nitrogen are recorded in percentages. The p_H of each sample is also

noted. When untreated cow's milk was fed, the greatest amount of soluble nitrogen was reached one and one-half hours after feeding. The subsequent fall in the soluble nitrogen level was gradual. After milk to which rennin had been added was fed, the greatest amount of soluble nitrogen was reached one-half hour after feeding. A study of the typical case (table 1) shows that this amount was present in the gastric contents for an hour or more.

After feeding evaporated milk, the greatest quantity of soluble nitrogen in the gastric contents was usually found in one-half hour, but occasionally in one hour. Thereafter, less soluble nitrogen was present in our samples. When rennin was added to the evaporated milk, no difference was observed, nor was the range of values for soluble nitro-

TABLE 2.—*Time After Ingestion of Food at Which the Quantity of Soluble Nitrogen Was Greatest*

Kind of Milk		Case 1	Case 2	Case 3	Case 4	Case 5
Untreated cow's milk	Trial 1, hours	1	1	1	1	1
	Trial 2, hours	1½	1	1	1½	1
Cow's milk and Junket	Trial 1, hours	½	½	1	1	½
	Trial 2, hours	½	½	2	1½	1
Evaporated milk	Trial 1, hours	½	½	1	½	1
	Trial 2, hours	½	½	1	½	½
Evaporated milk and Junket	Trial 1, hours	½	½	1	½	1
	Trial 2, hours	½	½	1	½	1
Powdered milk	Trial 1, hours	1	½	1½	1½	½
Powdered milk and Junket	Trial 1, hours	1	½	1½	1½	1
Lactic acid milk	Trial 1, hours	½	½	½	½	½
	Trial 2, hours	½	½	1		
Protein milk	Trial 1, hours	½	½	1	1	1
	Trial 2, hours	½	½	1	1	
Buttermilk	Trial 1, hours	½	½	½	½	½
	Trial 2, hours	½	½	½	½	

gen changed. Therefore, it was safe to assume that this source of rennin does not increase the digestion of evaporated milk in the human subject.

With powdered milk our results were variable, the time at which most soluble nitrogen was present in our samples of gastric contents ranging from one-half to one and one-half hours. The addition of rennin to this milk made no difference in the time after ingestion at which the greatest quantity of soluble nitrogen was found.

In all cases the soluble nitrogen of buttermilk reached its greatest concentration in the gastric contents in one-half hour and was followed by a very large drop in the nitrogen level at the next reading. After the ingestion of protein milk or of lactic acid milk the gastric contents contained the maximum quantity of soluble nitrogen in from one-half to one hour, and the drop in soluble nitrogen after this time was more gradual than in the case of buttermilk.

If one assumes that the time needed to produce the highest concentration of breakdown products of protein in the gastric contents is the time required for digestion to be most effectively accomplished, one may rate these milks in regard to speed of digestion as follows: (1) buttermilk and cow's milk and Junket; (2) protein milk, lactic acid milk, evaporated milk and evaporated milk and Junket; (3) powdered milk, and powdered milk and Junket; (4) untreated cow's milk.

COMMENT

The advantage in using such modified milks as evaporated milk for the feeding of infants has been reported in numerous clinical investigations.[6] Experimental work in vitro and in vivo shows that the modified milks are more digestible than untreated milk.[7] The studies reported in this paper confirm the results of previous investigators.

A comparison of these results with those which we previously found in vitro follows. Examination of table 1 shows that the p_H of the gastric contents after the feeding of nonacid milks is about 4.5 for the first two determinations, or for a period of at least one half hour. After the ingestion of acid milks, the high point of the p_H of the gastric contents is 4, and it is noted only ten minutes after ingestion. Thereafter, the p_H decreases, reaching a low point of about 1.7 one or two hours after feeding. Our previous experiments have shown that at a p_H of 4.5 the addition of rennin to untreated cow's milk increases its digestibility about five times. At this low acidity, the digestion of untreated cow's milk in artificial gastric juice containing no source of rennin is very slight. At lower p_H values the digestion of milk without rennin is more speedy than that of the same material at a p_H of 4.5. The addition of rennin does not increase the speed of digestion materially. If the speed of digestion is influenced by the p_H in the human subject as we have found it to be in vitro, the effect of the addition of rennin to the foods probably takes place during the first half-hour. The effect of adding rennin is obvious only in the case of untreated cow's milk and is not noticeable with evaporated milk and powdered milk. This may be because the normal stomach contains enough rennin to take care of the more slowly digested cow's milk.

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6. Leopold, J. S.: Experiences with Whey Modified Milk in Infant Feeding, Am. J. Dis. Child. **8**:196 (Sept.) 1914; Arch. Pediat. **27**:602, 1910. Springfield and Tobbey: Arch. Pediat. **27**:602, 1910. Marriott, M., and Schoenthal, L.: Arch. Pediat. **46**:135, 1929. Brennemann, J.: The Curd and the Buffer in Infant Feeding, J. A. M. A. **92**:364 (Feb. 2) 1929.

7. Mojonnier, T.: M. News **87**:877, 1905. Wallen-Lawrence, Z., and Koch, F. C.: Relative Digestibility of Unsweetened Evaporated Milk, Boiled Milk and Raw Milk by Trypsin in Vitro, Am. J. Dis. Child. **39**:18 (Jan.) 1930.

The correlation of the speed of formation of the maximum breakdown products of protein with the emptying time of the stomach after ingestion of the various milk foods will next be considered.

Our studies show that after buttermilk is fed the products of digestion are most quickly formed. Next in speed of digestion are protein milk, lactic acid milk, evaporated milk, and milk and junket. Then comes powdered milk, and, last of all, untreated cow's milk. If, then, the presence of the products of digestion influence the emptying time of the stomach, one would expect hunger contractions to appear first and most vigorously in the stomach of a subject who has been fed buttermilk. Similarly, one would expect hunger activity to show itself after the feeding of the different milks in the same order as the speeds of their digestion. Actually, we found that this is true. Gastric motor activity occurs soonest and most vigorously after ingestion of buttermilk and next after ingestion of the other acid milks. The stomach shows a more sluggish motility after the ingestion of nonacid milks and it is least active after untreated milk has been fed. The only inconsistent results were obtained with evaporated milk. We found in all cases a rapid digestion of evaporated milk, as revealed by the increase in soluble nitrogen and the late onset of hunger contractions following ingestion. Presumably, then, the rate of formation of the products of digestion cannot always be correlated with the emptying time of the stomach.

SUMMARY

Milk foods can be listed according to their speeds of digestion as noted by formation of breakdown products of protein in the following order: (1) buttermilk and Junket and cow's milk; (2) protein milk, lactic acid milk, evaporated milk and evaporated milk and Junket; (3) powdered milk and powdered milk and Junket; (4) untreated cow's milk.

The addition of rennin to nonacid modified milk in no way influences the speed of its digestion in vivo, except in the case of untreated cow's milk. The speed of digestion of untreated milk in vivo is greatly increased by the addition of rennin.

COMPARISON OF REACTIONS TO INTRACUTANEOUS AND SUBCUTANEOUS INJECTIONS OF DICK TEST TOXIN IN 653 CHILDREN

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The Dick test, performed to determine susceptibility to scarlet fever, consists of the intradermal injection of 0.1 cc. of the commercial toxin. The development of a nonindurated erythematous area measuring 10 by 10 mm. or more indicates susceptibility to the disease. To account for the discrepancies and difficulties that workers have experienced with the test, the Dicks [1] have listed a series of common sources of errors in the technic. One source of error listed is the subcutaneous instead of the intracutaneous injection of the toxin.

The purpose of the present investigation was to determine the validity of this point by actual trial, the work being carried out at the suggestion of Dr. Silber C. Peacock. The children tested were those admitted to the Children's Memorial Hospital for tonsillectomy and adenoidectomy. As a group they represented the average children of a dispensary clientele. They were selected by the staff of the Department of Medicine and admitted to the hospital for operation. The average stay in the hospital was approximately forty-eight hours. The tests were made during that period.

The testing material was standard commercial toxin, 0.1 cc. constituting a test dose. A well ground syringe graduated in tenths of a cubic centimeter and sharp 26 gage or 27 gage rustless steel needles were used. The needles and syringes were sterilized in an autoclave and dried there. Ether was used for cleansing the skin. The tests were made in duplicate, both forearms being used.

The intracutaneous test was performed in the usual manner, that is, the point of the needle was inserted into the skin and a wheal raised. After completion of the injection a wheal was left that was approximately 8 mm. in diameter, its surface usually pocked with small depressions.

The subcutaneous injection was made by thrusting the needle through the skin into the subcutaneous tissue. In doing this one could feel the needle pass through the skin and enter the subcutaneous layer. After the injection a small mound was left that in no way resembled the wheal produced by an intracutaneous injection.

Generally, positive reactions to the Dick test made near the wrist on the volar surface of the forearm result in a more circumscribed area of erythema than those made in the middle of the forearm. In order to eliminate the site as a possible

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1. Dick, G. F., and Dick, G. H.: The Control of Scarlet Fever, Am. J. Dis. Child. **38**:905 (Nov.) 1929.

factor responsible for differences in the reactions, in one half of the group of 653 children subcutaneous injections of the toxin were made on the volar surface of the forearm in the proximal segment of the middle third and the intracutaneous tests in the same third but distally. In the other half of the group, the sites of the tests were reversed. Thus, four separate tests were made for each child, a total of 2,612 tests being performed.

Readings were made in daylight. Occasional dark days made this difficult but were never a serious handicap. Measurements of the size of the erythematous areas were made with the aid of a draftsman's dividers and recorded as accurately as possible to the nearest millimeter. The reactions were classified as faint pink, bright red, swollen red or scarlatiniform.

In 636 (97.4 per cent) of the 653 children tested, the reactions to the four tests agreed. The difference or agreement in the size of

TABLE 1.—*Comparison of Reactions from Intracutaneous and Subcutaneous Injections of Toxin*

	Reactions		
Group 1	Positive	Negative	Total
Upper subcutaneous test	142	175	317
Lower intracutaneous test	142	175	317
Group 2			
Upper intracutaneous test	161	158	319
Lower subcutaneous test	161	158	319

TABLE 2.—*The average Dimensions of the Erythematous Areas*

Group 1	
Upper subcutaneous test	25 by 16 mm.
Lower intracutaneous test	23 by 18 mm.
Group 2	
Upper intracutaneous test	28 by 16 mm.
Lower subcutaneous test	22 by 15 mm.

the erythematous areas was found to be dependent on the location on the forearm rather than on the type of injection. If the sizes of the erythematous areas in the two sites were plotted, the resulting shapes would be an elongated ellipse for the proximal and a shorter or squat ellipse for the distal areas in the middle third of the forearm.

In 17 children the intracutaneous and subcutaneous injections did not give like results (table 3). From table 3 it will be noted that in 8 instances there was no reaction in one type of test as compared with a positive reaction of small dimension in the other type. It will be observed that there were actually three times as many positive reactions to the subcutaneous as to the intracutaneous injection, i. e., 6 of one to 2 of the other. In the remaining 9 tests, the difference between the diameter of the negative and those of the positive reactions were small, the average difference being only 8 mm. In the group of 17 children 14 of the subcutaneous tests were positive while the correspond-

ing intracutaneous tests were negative. Again, the intracutaneous tests were positive in 3 instances while their mates, the subcutaneous tests, were negative. The numerical superiority in positive reactions of the subcutaneous over the intracutaneous tests is relatively of little significance or interest and might disappear in another series.

TABLE 3.—*Data for Children Who Did Not Give Like Reactions to Both Tests*

Number	Intracutaneous Test	Subcutaneous Test
Group 1 (upper subcutaneous and lower intracutaneous tests)		
172	No reaction	13 by 11 mm.
178	No reaction	12 by 10 mm.
190	No reaction	12 by 10 mm.
192	6 by 5 mm.	10 by 10 mm.
223	10 by 10 mm.	6 by 6 mm.
313	11 by 10 mm.	No reaction
366	No reaction	14 by 12 mm.
Group 2 (upper intracutaneous and lower subcutaneous tests)		
8	7 by 7 mm.	14 by 11 mm.
10	7 by 9 mm.	14 by 11 mm.
11	5 by 6 mm.	11 by 10 mm.
13	4 by 2 mm.	12 by 11 mm.
14	5 by 2 mm.	11 by 10 mm.
40	No reaction	10 by 10 mm.
248	No reaction	10 by 10 mm.
251	8 by 8 mm.	16 by 14 mm.
254	7 by 7 mm.	11 by 10 mm.
542	14 by 12 mm.	No reaction

TABLE 4.—*Data for Children in Whom the Degree of Erythema and Type of Reaction Were Not Alike in All Four Sites*

Case	Injections	Types of Reaction: No Reaction	Faint Pink	Bright Red	Swollen Red	Scarlatiniform
372	Subcutaneous	1	1	..	..	..
	Intracutaneous	..	..	2	..	..
384	Subcutaneous	..	2	..	..	..
	Intracutaneous	..	1	1	..	..
474	Subcutaneous	..	2	..	..	..
	Intracutaneous	..	..	..	2	..
531	Subcutaneous	..	2	..	..	..
	Intracutaneous	..	1	1	..	..
631	Subcutaneous	..	..	..	..	2
	Intracutaneous	..	..	..	2	..
634	Subcutaneous	..	..	2	..	..
	Intracutaneous	..	..	..	2	..

Also, there was almost universal agreement as to the degree of erythema and the type of the reaction irrespective of the site of the test (table 4). Of the 303 children who reacted positively there were only 5 in whom the type of reaction differed in the four sites. It is of interest that in 5 of 6 children the intracutaneous test yielded the most pronounced type of reaction.

COMMENT

The data presented in this report tend to disprove the contention that it is necessary to be meticulous in delivering the toxin for the

Dick test intracutaneously in order to secure a maximum of positive reactions, since for practical purposes there is no difference between the results obtained by the two methods.

The sensitivity or reliability of the intracutaneous route for the injection of the toxin is in no way questioned. However, the data herein presented establish the fact that failure to obtain a positive reaction to an injection of toxin for the Dick test cannot justifiably be attributed to an inadvertent injection into the subcutaneous tissue.

Earle [2] expressed the opinion that deep intracutaneous injections of the toxin yield more positive reactions than do the more superficial injections. Apart from the fact that he mentioned in his report that in a few instances his deep intracutaneous injections were almost subcutaneous, this study has no bearing on his investigation.

This work is submitted with some reluctance because of the danger that hereafter the test may be performed without regard for the depth to which the needle is inserted and may result in an intramuscular injection of the toxin.

SUMMARY

1. Intracutaneous and subcutaneous injections of 0.1 cc. of toxin for the Dick test, each performed in duplicate, gave identical reactions in 636 (97.4 per cent) of 653 children.

2. The reactions obtained in 17 tests (2.6 per cent) did not agree. Of these there were 14 positive reactions to subcutaneous injections and 3 to intracutaneous injections with negative reactions in the duplicate tests.

3. There was agreement in all but 6 instances as to the degree of erythema noted.

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2. Earle, C. A.: Dick Test in Children, J. A. M. A. **103**:336 (Aug. 4) 1934.

EFFECT OF VACCINATION WITH BCG ON TUBERCULOSIS IN INFANCY AND IN CHILDHOOD

CORRELATION OF REACTIONS TO TUBERCULIN TESTS, ROENTGENOLOGIC DIAGNOSIS AND MORTALITY

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It has long been known that a primary tuberculous infection produces a resistance which modifies the course of a subsequent infection with the tubercle bacillus. Numerous attempts have been made to produce immunization against tuberculosis with products of tubercle bacilli and with tubercle bacilli killed by heat, light or chemicals or attenuated by drying, prolonged cultivation on artificial culture mediums or aging the culture. Attempts have also been made to immunize against the disease by means of acid-fast saprophytes and by means of tubercle bacilli which are nonpathogenic for the particular species. These efforts have never been wholly successful.

In 1906, Calmette and Guérin [1] claimed that resistance to tuberculosis could be induced by impregnating the lymphatic system with living, attenuated tubercle bacilli, which localize there and are incapable of producing generalized tuberculosis. Calmette and Guérin [2] believed that they had succeeded in modifying a strain of the bovine tubercle bacillus so that it no longer could produce generalized tuberculosis in susceptible animals but instead would induce resistance to reinfection with virulent tubercle bacilli. This culture, isolated in 1908 from the tuberculous udder of a cow and attenuated by repeated transplantations to mediums containing beef bile, has been designated BCG, or the bacillus of Calmette and Guérin.

At the present time the vast majority of investigators agree with Calmette and Guérin as to the attenuation of the BCG culture. On the other hand, a small group of investigators, among whom may be mentioned Petroff, Branch and Steenken,[3] Watson,[4] and Hutyra,[5] have

From the Henry Phipps Institute, University of Pennsylvania.

1. Calmette, A., and Guérin, C.: Ann. Inst. Pasteur **20**:609, 1906.
2. Calmette, A., and Guérin, C.: Ann. Inst. Pasteur **38**:371, 1924.
3. Petroff, S. A.; Branch, A., and Steenken, W.: Am. Rev. Tuberc. **19**:9, 1929.
4. Watson, E. A.: J. Vet. M. A. **71**:732, 1927.
5. Hutyra, F.: Ztschr. f. Immunitätsforsch. u. exper. Therap. **62**:74, 1929.

noted the occurrence of generalized tuberculosis in a small percentage of guinea-pigs inoculated with the BCG strain.

Park, Kereszturi and Mishulow [6] failed to increase the virulence of the BCG strain by the various methods suggested by different investigators. Cultures isolated from cold abscesses which developed in some children after the injection of BCG into the subcutaneous tissue were avirulent for rabbits and guinea-pigs.

The dissociation of the BCG strain into rough and smooth colonies, first demonstrated by Petroff, Branch and Steenken,[7] has been confirmed by numerous observers. Most of them, however, failed to observe generalized tuberculosis in animals inoculated with the dissociated colonies. Despite the fact that a million or more children have been vaccinated with this culture by many investigators, there is no report in the literature of an unequivocal case of generalized tuberculosis attributable to the BCG vaccine. Cantacuzène, Ciuca, Nasta, Veber and Alexa [8] concluded that in man the ingestion of the BCG vaccine induces a transient inflammatory reaction of the mesenteric lymph nodes, an increase of the reticulo-endothelial cells of the sinuses and an infiltration with polymorphonuclear cells, followed by formation of islets of connective tissue which, in turn, are absorbed, resulting in complete restitution of the tissue after from two to three months.

Many reports have been published [9] dealing with the value of BCG vaccine, the majority of which are based on the total number of infants vaccinated among the general population, with relatively little consideration of the rôle played by contagion. However, the results of vaccination for tuberculosis, as for other infectious diseases, can be evaluated only when the degree of exposure to the disease is taken into consideration. To determine more accurately the value of BCG vaccine a study was undertaken in which new-born infants residing in families with known cases of manifest tuberculosis were given the BCG vaccine orally, while infants similarly exposed but too old to be vaccinated by mouth when first observed in the clinic served as controls.

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6. Park, W. H.; Kereszturi, C., and Mishulow, L.: Effects of Vaccination with BCG on Children from Tuberculous Families, J. A. M. A. **101**:1619 (Nov. 18) 1933.

7. Petroff, S. A.; Branch, A., and Steenken, W.: Proc. Soc. Exper. Biol. & Med. **25**:14, 1927.

8. Cantacuzène, J.; Ciuca, M.; Nasta, M.; Veber, I., and Alexa, J.: Arch. roumaines de path. exper. et de microbiol. **2**:131, 1929.

9. Vaccination préventive de la tuberculose de l'homme et des animaux par le BCG. Rapports et documents provenant des divers pays (la France exceptée) transmis à l'Institut Pasteur en 1932, Paris, Masson & Cie, 1932. Kalbfleisch, H. K., and Nohlen, A.: Zentralbl. f. d. ges. Tuberk.-Forsch. **31**:433, 1929. Wileminsky, F. W.: ibid. **36**:497, 1932. Tiedemann, H. J.: ibid. **39**:433, 1934.

METHOD

The strain of BCG used in this study was obtained in 1928 from Dr. M. J. King, of the Metropolitan Life Insurance Company Sanatorium, Mount McGregor, New York. New equipment, including the incubator for culturing and preparing the vaccine, was used and kept under lock on a floor of the Institute not used for any other bacteriologic or pathologic studies. The culture was maintained continuously on Sauton's medium and on potato soaked in glycerin and veal broth. After ten transplantations on one or the other medium the culture was transferred to potato soaked in beef bile and transplanted two or three times before it was returned to the mediums free from bile. To determine the avirulence of the strain, 30 mg. of the fifth and of the tenth transplants of the culture was injected into the subcutaneous tissue of two guinea-pigs. These animals were kept under observation for three months, at the end of which time they were killed and necropsy was performed. Up to the present time this strain of BCG has produced no generalized tuberculosis in any of the inoculated guinea-pigs.

For human use the vaccine was freshly prepared for each infant from a culture not more than three weeks old, grown on Sauton's medium or on slants of veal broth and potato. The bacillary mass was dried between sterile filter papers and weighed, and a suspension was made containing 5 mg. of bacilli per cubic centimeter in a mixture of 4 per cent glycerin and 1 per cent dextrose in sterile water. At intervals of forty-eight hours the infants were fed three doses of 2 cc. each of the vaccine by means of a sterilized medicine dropper, each dose containing 10 mg. of BCG culture. The vaccination was completed in every instance before the infant was 10 days old. Since in almost every case the infants were born in a hospital and separated from the tuberculous member of the family, they remained free from exposure to tuberculosis during the ten to fourteen day period of hospitalization. The babies were subsequently examined when possible during the first three months and at intervals of three months during the first year and of six months thereafter. Tuberculin tests and roentgen examinations were made at varying periods of time. The vaccinated babies and the unvaccinated controls were subdivided into three groups: (1) those in contact with persons with tuberculosis whose sputum contained the tubercle bacilli; (2) those in contact with persons with tuberculosis whose sputum did not contain the tubercle bacilli; and (3) those not in contact with any persons known to have the disease.

Between December 1927 and October 1934, forty-three white and twenty-seven colored infants, from forty-one white and twenty-six colored families, were given 30 mg. of the BCG vaccine by mouth. As controls, one hundred and fourteen white and fifty-three colored infants, born between December 1927 and October 1934 into eighty-nine white and forty-one colored families, were studied.

MORTALITY FROM TUBERCULOSIS IN VACCINATED AND IN UNVACCINATED CHILDREN

In the first group, containing twenty-six white and fifteen colored children who had been vaccinated with BCG and were in contact with persons with tuberculosis whose sputum contained the tubercle bacilli, the average age at the time of the last examination was 31.4 months. In this group only one death from tuberculosis occurred; a 16 month old colored child died after having measles. The diagnosis of tuber-

culosis was based on increasing pulmonary infiltration demonstrated by repeated roentgenologic examinations.

The unvaccinated control group consisted of fifty-four white and thirty colored children who, like those in the vaccinated group, remained in contact with patients with tuberculosis whose sputum contained tubercle bacilli. The average age of this group at the time of the last examination was 40 months. Of this group of eighty-four babies, four white (7.4 per cent) and six colored (20 per cent) or a total of 11.9 per cent, died of miliary tuberculosis. One child died at the age of 4 months, three children at the age of 7 months, two at the age of 9 months and the remaining four at the ages of 10, 11, 13 and 30 months, respectively. In the cases of nine of the ten children the diagnosis was made by means of one or more roentgen examinations, and it was confirmed in five of the nine cases by necropsy. In the case of the tenth patient no roentgen examination was made, but tubercle bacilli were found in the spinal fluid.

In the second group, consisting of eleven white and four colored children who were vaccinated but remained in contact with tuberculous patients whose sputum had been persistently negative for tubercle bacilli, no deaths from tuberculosis occurred. The average age of this group was 28.3 months. Among the twenty-nine white and sixteen colored children of the unvaccinated control group similarly exposed, two colored children died, one at the age of 7 months and the other at the age of 11 months, from miliary and generalized lymphatic tuberculosis, respectively. The diagnosis in the case of the first patient was based on roentgenologically demonstrated lesions of the chest and necropsy and in the case of the second patient on biopsy of a cervical lymph node. The average age of this group of children was 39.3 months.

In the third group of children, those not exposed to persons known to have tuberculosis, no deaths from tuberculosis occurred among the six white and eight colored vaccinated children and thirty-one white and seven colored unvaccinated controls. The mortality from tuberculosis among the children vaccinated with BCG vaccine and among the unvaccinated children is presented in table 1.

Of the fourteen vaccinated children who were not exposed to tuberculosis, six died within the first two months from inanition or prematurity. These infants, born to mothers in advanced stages of tuberculosis, were separated from their mothers immediately after birth and subsequently institutionalized. Necropsy performed on two of the infants two months after vaccination with BCG vaccine failed to reveal any gross or microscopic evidence of tuberculosis, and cultures and inoculations of guinea-pigs with material from the mesenteric and the hilar lymph nodes, as well as from the spleen, gave negative results for tubercle bacilli.

REACTION TO TUBERCULIN

That the administration of the BCG vaccine produced sensitization to tuberculin was first clearly demonstrated by Debré and Cofino,[10] who placed vaccinated and unvaccinated children in surroundings free from tuberculosis and found that 88.6 per cent of one hundred and thirty-two vaccinated children 4 or less than 4 years of age reacted to tuberculin, while no positive reaction to tuberculin was observed among the one hundred and forty-one unvaccinated children.

In this study the vaccinated and unvaccinated babies were given intracutaneous tuberculin tests within the first few months of life when possible, at the age of 6 and of 12 months and at yearly intervals thereafter. The test was made by injecting 0.01 mg. of freshly diluted standardized old tuberculin into the skin of the forearm, and if no reaction was observed forty-eight hours later, 1 mg. of tuberculin was injected into the skin of the opposite arm. Readings were recorded in the manner descibed in a previous article.[11]

TABLE 1.—*Mortality from Tuberculosis in Children Vaccinated with BCG and in Unvaccinated Children*

	Exposed to Persons with Tuberculosis Whose Sputum Contained Tubercle Bacilli			Exposed to Persons with Tuberculosis Whose Sputum Did Not Contain Tubercle Bacilli			Not Exposed to Persons with Manifest Tuberculosis		
		Died of Tuberculosis			Died of Tuberculosis			Died of Tuberculosis	
	Total No.	No.	Percentage	Total No.	No.	Percentage	Total No.	No.	Percentage
Vaccinated	41	1	2.4	15	0	...	14*	0	..
Unvaccinated	84	10	11.9	45	2	4.4	38	0	..

* Diagnosis of manifest tuberculosis was not confirmed in seven instances, while in the remaining seven instances the mothers died of tuberculosis or remained in hospitals.

The reaction to tuberculin in very young infants differs somewhat from that in older children and adults, in that the edema is more sharply circumscribed, the induration more firm and the area of redness about the edema smaller and more pale.

The results of the tuberculin tests in both the children vaccinated with BCG and the unvaccinated children are presented in table 2. It will be observed from this table that the incidence of positive reactions to tuberculin in the first group of infants in contact with tuberculous persons whose sputum contained tubercle bacilli is not significantly different for the vaccinated and the unvaccinated children. In this group no conclusion can be drawn about the rôle played by BCG vaccine

10. Debré, R., and Cofino, E.: Ann. Inst. Pasteur **44**:12, 1930.

11. Aronson, J. D.: Am. J. Hyg. **14**:374, 1931.

in inducing a positive reaction to tuberculin, since the positive reaction may be the result of an exogenous infection with virulent tubercle bacilli. On the other hand, in the second group, those in contact with persons having tuberculosis whose sputum did not contain tubercle bacilli, as well as in the third, or unexposed group, the percentage of positive reactions to tuberculin is much lower among the unvaccinated children than among those vaccinated with BCG. It would seem, therefore, that the peroral administration of the BCG vaccine to infants under 10 days of age induces sensitivity to tuberculin in a high percentage of cases.

A comparison of the ages at which the reaction to tuberculin first became positive in the vaccinated and unvaccinated children cannot be made with any degree of accuracy, since many of the unvaccinated

TABLE 2.—*Reactions to Tuberculin in Children Vaccinated with BCG and in Unvaccinated Children*

		Positive Reactions to Old Tuberculin					
		To 0.01 Mg.		To 1 Mg.		Total	
	Number Tested	Number	Percentage	Number	Percentage	Number	Percentage
Exposed to Persons with Tuberculosis Whose Sputum Contained Tubercle Bacilli							
Vaccinated.....	38	25	66	6	16	31	82
Unvaccinated.....	79	49	62	14	18	63	80
Exposed to Persons with Tuberculosis Whose Sputum Did Not Contain Tubercle Bacilli							
Vaccinated.....	14	9	64	4	29	13	93
Unvaccinated.....	44	7	16	9	21	16	36
Not Exposed to Persons with Manifest Tuberculosis							
Vaccinated.....	8	3	38	3	38	6	75
Unvaccinated.....	38	4	11	5	13	9	24

children were not tested at an early age, their inclusion in the study being subsequent to and because of the discovery of tuberculosis in their households.

Among the thirty-one children vaccinated with BCG who reacted to tuberculin and remained in contact with persons with tuberculosis whose sputum contained the tubercle bacillus, twenty-three reacted within six months following vaccination. Of this group of thirty-one children, sensitivity to tuberculin increased in three, decreased in two and disappeared in three, at the ages of 44, 48 and 60 months, respectively. Of the sixty-two unvaccinated children who reacted to tuberculin and remained in contact with persons having tuberculosis whose sputum contained tubercle bacilli, sensitivity to tuberculin increased in three and disappeared in two, at the ages of 36 and 56 months, respectively.

Among the thirteen vaccinated children who reacted to tuberculin and who remained in contact with persons with tuberculosis whose sputum did not contain tubercle bacilli, nine reacted within six months

following vaccination. In two of the thirteen children who reacted, the reaction disappeared, at the ages of 52 and 58 months, respectively. Of the sixteen unvaccinated control children who reacted to tuberculin and remained in contact with tuberculous persons whose sputum did not contain tubercle bacilli, the reaction disappeared in four, at the ages of 28, 45, 66 and 69 months, respectively.

Among the six vaccinated children who reacted to tuberculin and were not in contact with persons having manifest tuberculosis, five reacted within six months after vaccination. Of these, one gave a negative reaction at the age of 33 months. Among the nine unvaccinated control children living under similar conditions who reacted to tuberculin, two reacted negatively at the ages of 64 and 72 months.

The intensity of the reaction to tuberculin was most marked in those of the unvaccinated control group who were in contact with persons having tuberculosis whose sputum contained tubercle bacilli. Of those who reacted to the injection of 0.01 mg. of tuberculin, 52.1 per cent gave a 3 plus (+++) reaction and 4.1 per cent, a 4 plus (++++) reaction. On the other hand, among the children vaccinated with BCG, 8 per cent gave a 3 plus reaction and none gave a 4 plus reaction. Among the vaccinated and unvaccinated children in contact with tuberculous persons whose sputum did not contain tubercle bacilli, as well as among those with no history of contact, the reaction to either 0.01 mg. or 1 mg. of tuberculin did not exceed 2 plus (++) in intensity.

RESULTS OF ROENTGENOLOGIC EXAMINATION

Roentgenologic examination was made of the chest of the children vaccinated with BCG within the first two or three months of life and at varying intervals thereafter. In a small group of children roentgenologic examinations of the abdomen also were made, but they gave negative results. The majority of the unvaccinated children were not examined at such an early age, since they were included in the study only after the demonstration of manifest tuberculosis in their families.

In four of thirty-six children vaccinated with BCG and in contact with persons with tuberculosis whose sputum contained tubercle bacilli, pulmonary infiltration was recognized by roentgenologic examination. In three of these a calcified node in the region of the hilus was subsequently observed; the fourth child died at the age of 16 months with extensive pulmonary infiltration. In two other children a calcified node only was observed in the region of the hilus, while in the remaining thirty children no roentgenologically demonstrable lesions were observed.

Of eighty-three unvaccinated children living in contact with persons having tuberculosis whose sputum contained tubercle bacilli, thirty-six showed no pulmonary lesions demonstrable by roentgen examination,

while forty-seven children presented roentgenologically recognizable lesions of the lungs or the hilar lymph nodes or both. In thirty-three of these forty-seven children, evidence of pulmonary infiltration was found by roentgen examination, in fifteen instances associated with an enlarged uncalcified node in the region of the hilus and in fourteen instances followed by calcification of the nodes in this region. In four patients infiltration was associated with questionable enlarged nodes in the region of the hilus. Of the remaining fourteen patients in whom pulmonary infiltration was not observed, ten were found to have a calcified node in the region of the hilus, two a calcified node and nodule and two an enlarged uncalcified node. The age at which these various lesions were first noted roentgenologically is presented in table 3.

TABLE 3.—*Age at Which Pulmonary Lesions Recognizable by Roentgenologic Examination Were Observed*

	Exposed to Persons with Tuberculosis Whose Sputum Contained Tubercle Bacilli							
	Vaccinated Children				Unvaccinated Children			
Age in Years	Infiltrations	Enlarged Nodes	Calcified Nodes	Negative Results	Infiltrations	Enlarged Nodes	Calcified Nodes	Negative Results
Under 1	0	0	0	8	17	8	0	6
1 to 2	4	0	1	4	8	4	1	5
2 to 3	1	0	0	6	10	2	10	6
3 to 4	1	0	2	6	6	3	7	8
4 to 5	0	0	1	3	1	2	4	5
5 to 6	0	0	1	2	1	0	1	7
6 to 7	0	0	0	1	0	0	2	0
Total	6	0	5	30	43	19	25	37

In marked contrast to the frequency with which lesions demonstrable by means of the roentgen rays were observed among the children in contact with persons with tuberculosis whose sputum contained tubercle bacilli, especially among the unvaccinated control group, is the infrequency of such findings among those in contact with persons with tuberculosis whose sputum did not contain tubercle bacilli. From thirteen of these children vaccinated with BCG, none presented roentgenologic evidence of pulmonary involvement, but of forty unvaccinated control children two showed roentgenologic evidence of a pulmonary lesion. In one of these children pulmonary infiltration was observed at 18 months of age and a calcified node at 36 months. In the other child pulmonary infiltration was observed at 7 months, and death from miliary tuberculosis occurred shortly after.

Among the vaccinated and unvaccinated children not in contact with manifest tuberculosis, no tuberculous pulmonary involvement was observed by means of the roentgen rays in either group.

CORRELATION OF REACTION TO TUBERCULIN WITH ROENTGENOLOGIC FINDINGS

A correlation of the results of the tuberculin tests with those of the roentgenologic examinations shows that of the thirty-six vaccinated children in contact with persons having tuberculosis whose sputum contained tubercle bacilli, the six children who presented roentgenologic evidence of the disease also gave a positive reaction to the injection of 0.01 mg. of tuberculin into the skin. Of the remaining thirty children with no roentgenologically demonstrable pulmonary lesions, eighteen reacted to the injection of 0.01 mg. of tuberculin and five to the injection of 1 mg. and seven failed to react to both doses.

Among the unvaccinated control children similarly exposed, forty-seven presented roentgenologic evidence of pulmonary involvement. Of this number, thirty-nine reacted to the injection of 0.01 mg. of tuberculin and two to the injection of 1 mg.; five died before receiving the test, and one failed to react to 1 mg. of tuberculin. On the other hand, of the thirty-six children of this group who presented no roentgenologic evidence of pulmonary involvement, thirteen reacted to the injection of 0.01 mg. of tuberculin, nine reacted to 1.0 mg. and fourteen failed to react to both doses of tuberculin.

Among the second group of children in contact with persons with tuberculosis whose sputum did not contain tubercle bacilli, two of the unvaccinated control group presented roentgenologic evidence of pulmonary involvement, and both of these children reacted to the injection of 0.01 mg. of tuberculin into the skin.

SOURCE OF INFECTION AND MORTALITY FROM TUBERCULOSIS

The relationship of a tuberculous member of a household to the other members must be considered in determining the spread of the disease, because of variations in degree of intimacy and in frequency of contact. The relationship of the member of the household suffering from tuberculosis to the exposed children is presented in table 4.

It will be observed in this table that the mother was the source of infection in a higher percentage of cases of the children vaccinated with BCG than of the unvaccinated children. In the cases of the latter group the father and other relatives constituted the greater source of infection. This difference was arrived at with the cooperation of several maternity hospitals in Philadelphia, which permitted us to vaccinate the babies of their tuberculous mothers. Relatively more mothers were a source of infection to vaccinated than to unvaccinated children.

In table 5 is presented the relationship of the patient who was the source of contact to the exposed child and the number and percentage of these patients who died of tuberculosis.

It was found that of eight white and thirteen colored primiparas, five white and eight colored women (61.9 per cent) died of tuberculosis

TABLE 4.—*Relations of Persons Who Were Source of Infection to Exposed Children*

	Exposed to Persons with Tuberculosis Whose Sputum Contained Tubercle Bacilli				Exposed to Persons with Tuberculosis Whose Sputum Did Not Contain Tubercle Bacilli				Not Exposed to Persons with Manifest Tuberculosis			
	Vaccinated Children		Unvaccinated Children		Vaccinated Children		Unvaccinated Children		Vaccinated Children		Unvaccinated Children	
Relationship to Child	No.	Percentage	No.	Percentage	No.	Percentage	No.	Percentage	No.	Percentage	No.	Percentage
Mother	21	55	20	29	14	93	9	26	7*	50	0	..
Father	14	37	30	43	0	..	14	40	0	..	0	..
Relative	3	8	20	28	1	7	12	34	0	..	0	..
No contact	0	..	0	..	0	..	0	..	7	50	30	100
Total	38	100	70	100	15	100	35	100	14	100	30	100

* Number of vaccinated children who died of tuberculosis soon after delivery or remained in the hospital.

TABLE 5.—*Mortality from Tuberculosis of Persons Who Were Source of Infection*

	Vaccinated Children			Unvaccinated Children		
Relationship to Child	Total Number	Number Who Died	Percentage	Total Number	Number Who Died	Percentage
Exposed to Persons with Tuberculosis Whose Sputum Contained Tubercle Bacilli						
Mother, primipara	9	5	56	8	4	50
Mother, multipara	12	5	42	12	7	58
Father	14	3	21	30	19	63
Relatives	3	3	100	20	9	45
No contact	0	0	..	0	0	..
Total	38	16	42	70	39	56
Exposed to Persons with Tuberculosis Whose Sputum Did Not Contain Tubercle Bacilli						
Mother, primipara	8	0	..	1	0	..
Mother, multipara	6	0	..	8	1	13
Father	0	0	..	14	0	..
Relatives	1	0	..	12	0	..
No contact	0	0	..	0	0	..
Total	15	0	..	35	1	3
Not Exposed to Persons with Manifest Tuberculosis						
Mother, primipara	4	4	100	0	0	..
Mother, multipara	3	1	33	0	0	..
Father	0	0	..	0	0	..
Relatives	0	0	..	0	0	..
No contact	7	0	..	30	0	..
Total	14	5	36	30	0	..

at intervals ranging from two weeks to twenty-six months after delivery, with an average of ten months. Of thirteen white and fifteen colored multiparas with tuberculosis whose sputum contained tubercle bacilli, four white and nine colored, a total of thirteen (46.4 per cent) died of

tuberculosis at intervals ranging from one to fifty-five months following delivery, with an average of twenty months. Of the multiparas with tuberculosis whose sputum did not contain tubercle bacilli, only one of seven died of pulmonary tuberculosis, eighteen months following delivery. These results, like many others, indicate the unfavorable influence of pregnancy and its sequelae on women who suffer from tuberculosis, and they are in accord with the observations of Norris and Landis,[12] who found that in about 20 per cent of quiescent and 70 per cent of advanced cases the tuberculous process was aggravated during pregnancy and the puerperium.

COMMENT ON OBJECTIONS TO USE OF BCG VACCINE

In estimating the value of the BCG culture as a protective vaccine in tuberculosis, it is necessary to take into consideration the attenuation of the BCG culture, its efficacy in giving protection against reinfection with virulent tubercle bacilli and the possible danger of the resulting allergy to the vaccinated child.

Some objections to the use of the BCG culture are based on the premise that if this culture is not completely attenuated or is not a virus fixé, it may increase in virulence and regain its original pathogenicity. Up to the present time the strain which we received in 1928 and used in this study, and which has been transplanted exactly as prescribed by Calmette,[13] has not been found pathogenic for either human beings or guinea-pigs. Lurie [14] has shown that in rabbits the BCG culture, serial no. 367, received by him in 1928 undergoes multiplication in all of the organs of the rabbit, followed later by rapid destruction of the culture in all of the organs except the lymph nodes, where it may persist for as long as fourteen months without producing any gross or microscopic lesions of tuberculosis and with no increase in virulence. On the other hand, in two of sixteen guinea-pigs inoculated with 10 mg. of another culture of BCG soon after its receipt in 1926 generalized tuberculosis developed. However, since these animals were kept in a room where numerous tuberculous animals were present and since they were all cared for by the same personnel, the possibility of spontaneous tuberculosis cannot be excluded. Since the receipt of this culture in 1926, it has been used only for experimental work on animals and has been transplanted repeatedly to glycerin agar without being returned to mediums containing bile. At the present time it produces generalized tuberculosis in a high percentage of inoculated guinea-pigs,

12. Norris, C., and Landis, H. R. M.: Pregnancy and Pulmonary Tuberculosis, J. A. M. A. **70**:362 (Feb. 9) 1918.

13. Calmette, A.: Ztschr. f. Tuberk. **50**:124, 1928.

14. Lurie, M.: J. Exper. Med. **60**:163, 1934.

and Lurie [15] observed generalized tuberculosis in a small percentage of rabbits infected with this strain. It is probable that the culture received in 1926 was not completely attenuated and that as a result of transplantations on mediums free from bile its pathogenicity has increased.

Numerous well controlled experiments on the animals ordinarily used in the laboratory, as well as cattle, have shown that the BCG vaccine is capable of inducing a certain degree of resistance to reinfection with virulent tubercle bacilli, and Griffith [16] found that in some monkeys a low grade of resistance was induced by the BCG vaccine. One of us observed that if guinea-pigs were vaccinated by injection of 5 mg. of attenuated BCG culture into the subcutaneous tissue and then reinfected six weeks later by intratracheal injection of a small number of virulent bovine tubercle bacilli, when killed six weeks after reinfection they presented enlargement and marked fibrosis of the hilar lymph nodes with only a few small tubercles in the spleen. On the other hand, guinea-pigs vaccinated with heat-killed tubercle bacilli, as well as the untreated control guinea-pigs, showed marked enlargement and caseation of the hilar lymph nodes with numerous tubercles throughout the spleen when they subsequently were infected with the same virulent culture in the same dosage.

The rôle played by vaccination with BCG in protecting human beings against reinfection is not so easily determined, because of the numerous uncontrollable factors which may influence the spread and course of the disease. Vaccination of alternate children in a household does not necessarily give an accurate measure of the value of the vaccine, since we have noted that in a group of unvaccinated children living in contact with persons having tuberculosis whose sputum contains tubercle bacilli only occasionally does more than one child in such a household die of tuberculosis, although the remaining children are usually infected, as shown by a positive reaction to tuberculin or positive roentgen ray findings in the chest or both.

Stewart [17] has stated that the immunization of children with BCG vaccine is objectionable because the resulting allergy favors, on reinfection, the development of the adult type of tuberculosis. According to Myers and Harrington,[18] 9 per cent of children who reacted to tuberculin in 1921 and 1922 were found to have clinical tuberculosis either at

15. Lurie, M.: J. Exper. Med. **55**:31, 1932.

16. Griffith, A. S.: Studies of Protection Against Tuberculosis: Results with B.C.G. Vaccine in Monkeys, Medical Research Council, Spec. Rep. Ser. 152, London, His Majesty's Stationery Office, 1931.

17. Stewart, C. A.: Does Primary Tuberculous Infection Afford Adequate Protection Against Consumption? J. A. M. A. **100**:1077 (April 8) 1933.

18. Myers, J. A., and Harrington, F. E.: Effect of Initial Tuberculous Infection on Subsequent Tuberculous Lesions, J. A. M. A. **103**:1530 (Nov. 17) 1934.

the time of the initial examination or when recently reexamined, while only 1 per cent of those who failed to react to tuberculin acquired clinical tuberculosis. They concluded that the marked difference in the incidence of clinical tuberculosis in the two groups is due to the allergy resulting from the primary infection.

If this concept is correct, it is difficult to explain why children infected with the tubercle bacillus within the first few years of life and repeatedly reinfected usually fail to have clinical tuberculosis until they reach their teens. Similarly, it is difficult to explain on the basis of allergy why in Philadelphia, where the incidence of tuberculous infection in adults ranges between 80 and 90 per cent, only about 1 per cent suffer from manifest tuberculosis. Our own interpretation of the data presented by Stewart [17] and by Myers and Harrington [18] would be that the development of clinical tuberculosis in those who reacted to tuberculin might be due to more or less continued exposure to the tubercle bacillus and that those who failed to react to tuberculin in the first place might not have experienced intense exposure.

The results obtained in various animals by the numerous investigators who have studied the question of vaccination with virulent or avirulent strains of tubercle bacilli definitely prove that a primary infection with the tubercle bacillus results in a certain degree of resistance to reinfection.

While Calmette [19] believed that children should be revaccinated with BCG vaccine in order to maintain their resistance, it seems to us to be an unnecessary procedure, since children exposed to tuberculous persons whose sputum contains tubercle bacilli are being infected repeatedly with variable amounts of viable, virulent tubercle bacilli, which according to many observers bring about a greater degree of resistance than can be attained with attenuated strains of the tubercle bacillus.

SUMMARY

Of forty-one children who remained in contact with persons having tuberculosis whose sputum contained tubercle bacilli and were vaccinated within the first ten days of life by the peroral administration of BCG vaccine, one (2.4 per cent) died of tuberculosis, while of eighty-four unvaccinated children living under comparable conditions, ten (11.9 per cent) died from the disease. Of fifteen children who remained in contact with persons with tuberculosis whose sputum did not contain tubercle bacilli and were vaccinated with the BCG vaccine, none died of tuberculosis; of forty-five unvaccinated children living under comparable conditions, two (4.4 per cent) died of tuberculosis. No deaths

19. Calmette, A.: L'infection bacillaire et la tuberculose, ed. 3, Paris, Masson & Cie, 1928.

from tuberculosis occurred in the children studied who were not exposed to persons known to have manifest tuberculosis, either among the fourteen children vaccinated with BCG or among the thirty-eight unvaccinated ones.

Of children in contact with tuberculous persons whose sputum contained tubercle bacili, 81.6 per cent of thirty-eight vaccinated children and 78.5 per cent of seventy-nine unvaccinated children reacted positively to an intracutaneous injection of tuberculin into the skin. Among fourteen vaccinated and forty-four unvaccinated children in contact with persons having tuberculosis whose sputum did not contain tubercle bacilli, 92.8 per cent of the vaccinated and 36.4 per cent of the unvaccinated children reacted to tuberculin. Among children who were not in contact with persons known to have tuberculosis, 75 per cent of eight vaccinated and 23.7 per cent of thirty-eight unvaccinated children reacted to tuberculin.

Of children living in contact with tuberculous persons whose sputum contained tubercle bacilli, 16.6 per cent of thirty-six children vaccinated with BCG and 56.6 per cent of eighty-three unvaccinated children present roentgenologically demonstrable lesions in the lungs. Among the children living in contact with persons with tuberculosis whose sputum did not contain tubercle bacilli, no pulmonary lesions demonstrable by the roentgen rays were observed in the thirteen who had been vaccinated, but 5 per cent of the forty unvaccinated children presented roentgenologic evidence of pulmonary lesions. No lesions demonstrable by means of the roentgen rays were found in the eight vaccinated or thirty-six unvaccinated children not in contact with persons known to have tuberculosis.

These results indicate that the administration of BCG vaccine to new-born children exposed to patients with manifest tuberculosis may prove of value in reducing the mortality from this disease in infancy and childhood.

The BCG culture used for vaccination in this study has remained attenuated for both human beings and guinea-pigs when maintained according to the method prescribed by Calmette.

Miss Margaret Smith and Miss Emma Du Four of The Henry Phipps Institute assisted during the course of this study, and Dr. R. S. Stephenson, Miss Helen Murphy and Miss Edith Erickson of the Philadelphia General Hospital cooperated in this work. Dr. F. Maurice McPhedran interpreted the roentgenograms.

TUBERCULOSIS IN CHILDHOOD

COMPARATIVE VALUE OF THE CUTANEOUS TESTS AND ANALYSIS OF HISTORIES OF CONTACT

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The present study was undertaken for a twofold purpose: (1) to analyze histories of contact, not only comparing the incidence of tuberculosis in the children of tuberculous families with the corresponding incidence in children in healthy families but also analyzing separately the relative significance of the specific types of contacts, and (2) to compare the reactions to cutaneous tests with each other and with clinical and roentgen findings, stressing the value of the Loewenstein test. This comparative study in conjunction with the family history is, I believe, the first work in English to be presented.

MATERIAL AND METHOD

The material consisted of a group of 1,207 children, 325 Negro and 882 white, who were referred to my associates and me because of a family history of tuberculosis and a history of contact with tuberculous persons. As controls we subjected a group of 50 Negro and 200 white children from healthy families to a similar study.

This work was begun in 1929. As each child appeared for study, the family history and the history of contact were verified by investigation in the home, consultation with the family physician or examination of the person with whom the patient had come in contact. Loewenstein, Mantoux and Pirquet tests were carried out on the children; roentgenograms of the chest were made and a thorough clinical examination was performed. The data were then subjected to statistical analysis.

In interpretation of reactions to the Mantoux test the old nomenclature of positive, slightly positive and negative was used during the early stages of the study. Subsequently this was replaced by one plus, two plus, three plus and four plus. In the summaries, reactions noted as positive under the old nomenclature and as three or four plus under the new were classified as definitely positive,

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The findings reported in this paper were taken from the files of the department of health of Newark. At the time the tests and readings were carried out there was no thought of using the material for the preparation of such a report as this. The tests were carried out as a routine under my direction and were read by physicians in the clinic who were accustomed to make such readings. All cases which came within the scope of this subject from 1929 to 1934 were included, and there was no selection of material beyond this. The original record cards are available for inspection in the department of health.

while slightly positive reactions under the old and 1 or 2 plus reactions under the new system were classed as slightly positive.

The significance of a negative cutaneous reaction has long been known. It generally rules out the possibility of tuberculous infection. However, the more serious problem arises in interpreting the positive reaction to tuberculin. Here the sensitiveness of the Mantoux and Pirquet tests is really a defect. In the determination of sensitiveness our rule is this: The smaller the proportion of positive responses, the less sensitiveness. A test which is too sensitive, such as the Mantoux test, causes too many false positive reactions, which are alarming, misleading and confusing. Other things being equal, therefore, the fewer the positive reactions, that is, the less sensitive a test is, the more useful it is when it does cause a positive response. Obviously, the reverse is true when negative reactions are being evaluated. Then, the more positive reactions caused by the test, the more significant is the negative response. At the moment the important problem is to find a less sensitive test; the Mantoux test serves well enough when it causes a negative response. What is needed is a less sensitive test, a positive reaction to which will have some significance.

TABLE 1.—*Results of Tests with Old Tuberculin*

	Mantoux			Pirquet			Loewenstein		
	Negative	Slightly Positive	Positive	Negative	Slightly Positive	Positive	Negative	Slightly Positive	Positive
White children									
Number	478	71	229	567	55	159	591	27	119
Percentage	61	9	30	73	7	20	80	4	16
Negro children									
Number	132	50	117	154	20	135	216	12	28
Percentage	44	17	39	49	7	44	84	5	11
All children tested		Number			Number			Number	
White		778			781			737	
Negro		229			309			256	

THE PIRQUET AND MANTOUX TESTS

In performing the Pirquet test we used undiluted old tuberculin and graded the reaction as positive, slight and negative. We used 0.1 cc. of a 1:1,000 solution of tuberculin for the Mantoux test. The classification of the Mantoux readings has already been described.

As will be seen in table 1, among the white children the reaction to the Mantoux test was positive in 30 per cent and that to the Pirquet test in 20 per cent. Among the Negro children the reaction to the Mantoux test was positive in 39 per cent, and the reaction to the Pirquet test in 44 per cent. With our criterion of the reaction to sensitiveness, therefore, one must conclude that among white children the Pirquet test is less sensitive and is therefore less likely to cause a false positive reaction. Among the Negro children the sensitivity of the tests was about the same. It should be noted that in both groups the Pirquet test caused a lower percentage of the confusing and indeterminate "slightly positive" reactions. The significance of the Loewenstein test will be discussed later, but it is worthy of note that this test caused fewer

slightly positive (indeterminate) responses than either of the other two and a decidedly lower number of positive responses, so that the chance of an indeterminate or false positive reaction would appear to be less with this test than with either the Pirquet or the Mantoux test.

These mass figures are generally satisfactory for reaching broad general conclusions as to the relative efficacy of the tests considered. However, a detailed analysis of the reactions of children who received both tests will demonstrate this more accurately. Such a comparison is presented in tables 2 and 3. If one assumes that a negative reaction to the Mantoux test (which caused the lowest proportion of negative reactions in each group) always indicates freedom from tuberculous infection, the question arises: How likely is one to be misled by finding positive Pirquet reactions in the group of children having negative Mantoux reactions? As is demonstrated in table 2, among white children the chance of such an error is considerably less than the likelihood of the reverse error, i. e., positive Mantoux reactions in children with a

TABLE 2.—*Comparison of the Reactions of White Children to the Mantoux Test with Their Reaction to the Pirquet Test*

	Children with a Positive Mantoux Reaction	Children with a Negative Mantoux Reaction
Positive Pirquet reaction, percentage	54	6
Negative Pirquet reaction, percentage	35	90
Slightly positive Pirquet reaction, percentage	11	4

negative Pirquet reaction. This tends again to confirm the conclusion that a negative reaction to the Mantoux test almost definitely rules out tuberculous infection. On the other hand, a negative reaction to the Pirquet test does not perform the same service, for 14 per cent of both the white and the Negro children having a negative Pirquet reaction had a positive Mantoux reaction.

The wide divergence between the reactions of the Negroes and those of the white children is worthy of note. It would appear that if in a white child the Mantoux reaction is negative the Pirquet reaction is not likely to be positive. Does it also follow that if the reaction to the Pirquet test is negative the Mantoux test is not likely to cause a divergent response? As indicated in table 4, this conclusion is not tenable. As I have already stated, the chief virtue of the Pirquet test is that it is less likely to cause a false positive reaction, but it is more likely, as suggested in tables 2, 3 and 4, to cause a spurious negative reaction.

From table 4 it is clear that a negative reaction to the Pirquet test is no indication that the reaction to the Mantoux test will also be negative; in fact, of every seven children giving a negative Pirquet reaction, one (i. e., 14 per cent) gave a positive reaction to the Mantoux test.

Contrast this with the data in table 2, in which it appears that of the white children giving a negative Mantoux reaction only 6 per cent gave a positive Pirquet reaction.

Another method of comparing these two tests is to analyze the proportion of positive responses of each age group. This is done in table 5. Among the white children the Mantoux test showed a greater incidence of positive responses at every age level. Among the Negroes, however, the relative proportion of positive responses varied considerably from age to age; the reaction to the Pirquet test was positive more often in the younger children, and the reaction to the Mantoux test,

TABLE 3.—*Comparison of the Reactions of Negro Children to the Mantoux Test with Their Reactions to the Pirquet Test*

	Children with a Positive Mantoux Reaction	Children with a Negative Mantoux Reaction
Positive Pirquet reaction, percentage	83	20
Negative Pirquet reaction, percentage	12	74
Slightly positive Pirquet reaction, percentage	5	6

TABLE 4.—*Comparison of the Reaction to the Pirquet Test with the Reaction to the Mantoux Test*

	Children with a Positive Pirquet Reaction	Children with a Negative Pirquet Reaction
Positive Mantoux reaction		
White, percentage	81	14
Negro, percentage	80	14
Negative Mantoux reaction		
White, percentage	18	86
Negro, percentage	20	86
Slightly positive Mantoux reaction		
White, percentage	1	0
Negro, percentage	0	0

in children over 11 years. Attention is also called to the fact that the constant annual rise in the proportion of positive responses to tuberculin is not found in this series. Of course, our group was somewhat selected, since the children came largely from families with tuberculous adults. These comparisons, therefore, have no absolute value as an indication of the incidence of tuberculous infection among children at various ages, their significance being limited to a contrast of the reactions to one cutaneous test with those to another within this specially selected group.

This study tends to confirm the generally accepted view that roentgenograms of the chest have little value in the diagnosis of tuberculosis in childhood. I found positive roentgen evidence in 4 per cent of the

children giving a positive reaction to the Mantoux test, in 2 per cent of those giving a negative reaction to the Mantoux test, in 6 per cent of those giving a positive reaction to the Pirquet test and in 4 per cent of those giving a negative reaction to the Pirquet test. On the other hand, of the children who did have positive roentgen findings, 58 per cent gave a positive reaction to the Pirquet test and 65 per cent gave a positive reaction to the Mantoux test. This suggests, although somewhat inadequately, that a spurious negative reaction is more likely with a Pirquet than with a Mantoux test.

Twenty-seven per cent of the children giving a positive reaction to the Mantoux test showed physical signs of tuberculous infection, and 19 per cent of those giving a negative reaction showed physical signs of tuberculosis. Of the children giving a positive reaction to the Pirquet test, however, one third showed some suspicious clinical findings on examination of the chest. Of the children with suspicious findings in the chest, 39 per cent gave a positive reaction to the Mantoux test, but only 22 per cent gave a positive reaction to the Pirquet test. As has been repeatedly pointed out in the literature, however, clinical examination of the chest is of uncertain value in the diagnosis of tuberculosis of childhood.

THE LOEWENSTEIN TEST

While the value of a negative reaction to the Mantoux or Pirquet test cannot be doubted, it is unfortunately true that most of my patients gave a positive response. Even if it is true, as many workers contend, that a positive reaction to tuberculin indicates an infectious focus, this fact is of little practical use. One cannot institutionalize, for example, all children showing a positive reaction to a cutaneous test, nor can one permit the roentgen or the clinical examination to decide whether a child needs care in a sanatorium or other special treatment. What is seriously needed in this work is some test less sensitive than the Pirquet or the Mantoux tests, yet sufficiently sensitive to point out all definite cases of tuberculosis of childhood. Such a procedure is, I believe, available in the Loewenstein test.

In this test a serum is used which was devised by Prof. E. Loewenstein of Vienna. It contains the soluble substance of the tubercle bacilli and whole dead bacilli, extracted with glycerin. Papers in the foreign literature have reported some success in the use of this serum for the treatment of tuberculosis. I have had, however, no personal experience with it as a therapeutic agency, my utilization of the material being confined to its employment for diagnosis. In procedure, the test is of the inunction type and is exceedingly simple to perform. One drop of the material is placed on the previously cleansed skin and is rubbed in vigorously until absorbed. The response is read in twenty-four, forty-eight and, if necessary, seventy-two hours. If a nodule appears at the

site of the inunction on any of these readings, the reaction is classified as positive. If the response is negative the patient is subjected to another test eight or ten days later. An intermediate response which must be classed as slightly positive is occasionally noted. In over 95 per cent of my cases, however, the reaction could readily be classified as negative or definitely positive.

In table 1 it will be noted that the Loewenstein test caused fewer positive responses than either of the others. Among white children only 16 per cent gave a positive reaction to the Loewenstein test, whereas 30 per cent gave a positive reaction to the Mantoux test. Among the Negroes the incidence of positive reaction to the Mantoux test was almost 40 per cent, whereas a positive reaction to the Loewenstein test

TABLE 5.—*A Summary of the Reaction to the Mantoux, Pirquet and Loewenstein Tests According to Age*

Age, Years	White			Negro		
	Mantoux	Pirquet	Loewenstein	Mantoux	Pirquet	Loewenstein
	Percentage*			Percentage*		
1	35	28	4	50	60	0
2	29	28	4	50	58	0
3	28	15	0	44	47	0
4	33	22	7	23	26	6
5	26	21	2	40	55	0
6	25	22	4	30	54	0
7	34	24	4	30	45	8
8	32	17	3	32	47	4
9	20	8	4	41	33	4
10	33	24	3	45	50	8
11	22	17	2	40	45	6
12	28	19	5	40	40	12
13	36	17	5	31	31	0
14	35	8	0	40	20	11
15	31	30	0	50	75	0

* The percentages indicate the proportion of positive responses.

was found in only 11 per cent. It will be noted also that slightly positive reactions, always indeterminate and unsatisfactory, appeared relatively rarely when the Loewenstein test was used. Among white children the proportion of slightly positive reactions was 9 per cent to the Mantoux test and only 4 per cent (less than half) to the Loewenstein test. Among the Negroes the proportions were 17 and 5 per cent, respectively. From these figures alone it would appear that the Loewenstein test satisfies the criterion of sensitiveness; it is manifestly less sensitive than either the Pirquet or the Mantoux test and accordingly is much less likely to cause a false positive reaction. I have used this test on 993 children in this study.

In every age group the proportion of positive reactions to the Loewenstein test was smaller than the incidence of positive reactions to the Mantoux or Pirquet test in that age group. This is indicated clearly in table 5.

The consistency with which the Loewenstein test less frequently caused a positive reaction than the other two tests strongly suggests that the procedure is relatively less sensitive and, accordingly, that it means more when it causes a positive response.

When, in a subsequent paragraph, I analyze the history of contact I shall again demonstrate that the proportion of positive reactions to the Loewenstein test fell below that of positive reactions to the Mantoux and Pirquet tests in every familial-history group.

Two questions, however, arise: (1) Does a negative reaction to the Loewenstein test exclude the possibility of tuberculous infection? (2) Does a positive reaction to the Loewenstein test mean exclusion of the need for giving a Mantoux or Pirquet test? To consider the second

TABLE 6.—*Incidence of Positive Reactions to the Mantoux and Pirquet Tests in Persons with a Positive Reaction to the Loewenstein Test*

White patients	
Positive Loewenstein reaction	
	94% had a positive Mantoux reaction
	97% had a positive Pirquet reaction
Slightly positive Loewenstein reaction	
	60% had a positive Mantoux reaction
	59% had a positive Pirquet reaction
Positive Mantoux reaction	
	45% had a positive Loewenstein reaction
Positive Pirquet reaction	
	63% had a positive Loewenstein reaction
Negro patients	
Positive Loewenstein reaction	
	96% had a positive Mantoux reaction
	85% had a positive Pirquet reaction
Slightly positive Loewenstein reaction	
	75% had a positive Mantoux reaction
	85% had a positive Pirquet reaction
Positive Mantoux reaction	
	58% had a positive Loewenstein reaction
Positive Pirquet reaction	
	69% had a positive Loewenstein reaction

question first, it should theoretically be true that if the frequency of positive reactions to the Mantoux or Pirquet test always exceeds that of positive reactions to the Loewenstein test, the reaction to the Mantoux or Pirquet test should always be positive in a patient in whom the reaction to the Loewenstein test is positive. To prove the truth of this I analyzed separately each case in which a Loewenstein test was carried out and found that substantially the theory is correct (table 6).

In almost every child in whom the Loewenstein reaction was positive the Mantoux reaction was also positive, and in the white children a positive Loewenstein reaction nearly always meant a positive Pirquet reaction. Among the Negro children this correlation was less clear. Stress should be laid on the observation that only 45 per cent of the patients giving a positive reaction to the Mantoux test also gave a positive reaction to the Loewenstein test. Apparently more than half the children giving a positive reaction to the Mantoux test therefore

did not have enough tuberculous infection to give a positive response to the Loewenstein test. As one might expect, the Pirquet test caused fewer of the false positive reactions: Sixty-three per cent of those who had a positive reaction to the Pirquet test gave a positive reaction to the Loewenstein test; so the fact that only a third of the children giving a positive reaction to the Pirquet test were not suffering from enough infection to give a positive reaction to the Loewenstein test made it substantially unnecessary to perform a Mantoux or Pirquet test, particularly in a white patient. Since only from 11 to 16 per cent of this highly selected group of children with tuberculous contacts gave a positive reaction to the Loewenstein test, we suggest that this test offers a good gage of the need for care in a sanatorium; when the reaction to the Loewenstein test is positive the child should be entitled to this special care, and when it is negative, the child should be kept under ambulatory observation.

It will be recalled that positive roentgen evidence was found for only 4 per cent of the children giving a positive reaction to the Mantoux test and in 6 per cent of those giving a positive reaction to the Pirquet test. Among the group giving a positive reaction to the Loewenstein test the proportion with positive roentgen findings was much higher, 16 per cent. It will also be recalled that positive clinical signs were reported in 27 per cent of the children giving a positive reaction to the Mantoux test and in 33 per cent of those giving a positive reaction to the Pirquet test. Almost 40 per cent of those giving a positive reaction to the Loewenstein test had evidence in the chest that was clinically suggestive of tuberculosis. This tended to confirm the pathognomonic value of a positive reaction to the Loewenstein test.

I return now to the first question: Does a negative reaction to the Loewenstein test rule out the possibility of tuberculous infection? I do not believe that this study permits me to draw any such conclusion. Ordinarily the criterion of excluding a diagnosis of tuberculous infection is a negative reaction to the Mantoux test. But as can be seen from table 6, from a third to a half of the children giving a positive reaction to the Mantoux test had a negative reaction to the Loewenstein test. If one assumes that a negative reaction to the Mantoux test is the only method of excluding tuberculous infection it would be obvious that a negative reaction to the Loewenstein test cannot serve such a purpose. But there is no other technic for testing for tuberculosis of childhood. Clinical signs, family history and roentgenograms are not of significant value in excluding a diagnosis of tuberculous infection. In the absence of any method of excluding such a diagnosis, I cannot see how one can interpret a negative reaction to the Loewenstein test. All I can say is that there was little evidence of the presence of tuberculosis of childhood other than a positive reaction to the Pirquet or Mantoux test

in the group of patients giving a negative reaction to the Loewenstein test. We are not prepared to state that the Mantoux test can be abandoned. However, we suggest that the Loewenstein test be performed first and as a routine procedure. It is simple and rarely arouses the objection on the part of parents that those cutaneous tests do which require the use of a needle, and if the reaction is positive therapeutic measures can be instituted without recourse to the other tuberculin tests, which will almost certainly elicit a positive reaction.

HISTORY OF CONTACT WITH TUBERCULOUS PERSONS

From the point of view of both the pediatrician and the public health worker, the uncovering of contacts with tuberculous persons is a matter of major importance. There are, in general, two methods of analyzing contacts. One is to begin with the definitely tuberculous child and go back to the family and discover the number of contacts; the other is to begin with tuberculous families and find the number of tuberculous children. I suggest that the latter is a more accurate and more useful technic. If the original tuberculous patient is taken as the starting point, there is no norm, no method of setting up a control unit. For example, at the Philadelphia Tuberculosis Conference, in November 1932, Wiesner and Smith [1] read a paper on this subject. They found that 15 per cent of the persons with whom tuberculous patients had come in contact were tuberculous. Now, this figure is interesting but of doubtful statistical value; one does not know how many tuberculous families there are in the community or how many persons are working and walking about with tuberculosis; one cannot tell, therefore, whether this incidence of 15 per cent of tuberculosis among persons with whom patients had come in contact is higher or lower than a control figure; in fact, no control figure is possible. A better method, I believe, is to take a group of families in which there is tuberculosis and determine the number of tuberculous children. If there are more tuberculous children, proportionately, among families containing tuberculous adults than among families of healthy adults, the influence of contact with a tuberculous person is statistically established.

As an instance of this type of study I recall the work of Evarts, Potter, and Dunn [2] and the earlier work of Opie and McPhedran [3] and of Chadwick.[4]

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1. Wiesner, D. E., and Smith, S. M.: Tuberculosis Clinic and Contact Study, Am. Rev. Tuberc. **29**:170 (Feb.) 1934.

2. Evarts, Helen; Potter, Rosalind, and Dunn, Emily: Tuberculosis Among the Children of Tuberculous Parents, Am. Rev. Tuberc. **29**:123 (Feb.) 1934.

3. Opie, E. L., and McPhedran, F. M.: Contagion of Tuberculosis, Am. Rev. Tuberc. **14**:347, 1926.

4. Chadwick, H. D.: Tuberculosis Case Finding, Tr. Nat. A. Prev. Tuberc. **15**:601, 1927.

Evarts and her associates found, for example, that of 451 children of tuberculous families, 42 or 9½ per cent subsequently had tuberculosis. This incidence is, of course, much higher than the incidence of tuberculosis generally. The conclusion was: "Tuberculosis mortality, 15-39 years, was between two and three times as high among offspring of white tuberculous parents in an industrial group as in the general white industrial population."

Most of the studies of this sort, however, are limited because only a relatively small number of cases are reviewed, and most authors have failed to indicate the specific type of contact, that is, the subject's relationship to the tuberculous adult. The work reported here represents

TABLE 7.—*A Comparison of the Reaction to Tests with Tuberculin in the Various Contact Groups*

White Patients	Negro Patients	Relationship* History of Tuberculosis	Positive Mantoux Reaction, Percentage		Positive Loewenstein Reaction, Percentage		Positive Pirquet Reaction, Percentage	
			White	Negro	White	Negro	White	Negro
199	49	None	17	30	11	6	10	24
111	56	Mother	25	38	9	13	22	40
32	53	Mother died	35	52	20	23	31	68
242	37	Father	28	35	12	0	20	41
91	31	Father died	52	49	29	14	37	56
56	18	Sister	27	16	8	6	21	44
12	12	Sister died	25	50	8	10	26	30
57	21	Brother	35	28	19	16	21	24
10	4	Brother died	50	75	30	25	50	50
13	11	Uncle	58	18	34	0	25	64
11	4	Aunt	40	75	40	0	17	100
6	7	Cousin	50	14	0	0	16	14
9	4	Boarder	56	100	56	0	33	100
6	4	Grandmother died	50	50	0	25	16	50

* Other groups such as those of an uncle or aunt who died of tuberculosis or a grandparent or stepparent who had or died of tuberculosis, are represented in the study, but as there were fewer than 10 in each such group, they are not included in this table.

an effort to avoid both of these defects. The study included more than 1,200 children, and the nature of the contacts has been analyzed.

In table 7 it will be noted that a positive reaction to the Mantoux test was found in 17 per cent of the white children in the control group and a positive reaction to the Pirquet test in 10 per cent of the same group. Surprisingly, the incidence of positive reactions to the Loewenstein test was greater than that of positive reactions to the Pirquet test. This is probably due to the fact that the control group was not an unselected set of healthy children but a group of school children referred because of cough or some similar symptom, coming from healthy family stock. It must be understood that the group with an irrelevant family history was a control only for the purposes of comparing contacts and family histories and not for the purpose of determining the absolute norm of distribution of positive reactions to the tuberculin tests.

We adopted the following formula for determining the significance of the contact: When the proportion of positive responses in the contact group exceeds the corresponding proportion in the control group by more than 50 per cent the finding is significant. Thus, 30 per cent of the Negro controls gave a positive reaction to the Mantoux test. We required, therefore, that the incidence of positive reactions to the Mantoux test in a special contact group be at least 45 per cent before it could be designated as significant. This requirement served to eliminate the chance variations which are inevitable in a study of this kind. We have also felt that no group containing fewer than ten subjects should be used as a basis for computing percentages of positive responses; accordingly, all groups of fewer than ten subjects were excluded from table 7. In drawing conclusions we have used only groups of fifty or more subjects.

With these limitations in mind we may reexamine table 7. The incidence of positive reactions to the Mantoux test in the white control group was 17 per cent, so that in accordance with the formulation a frequency of 25 per cent or more is significant provided the group numbers 50 or more subjects. There were 111 white children whose mothers had tuberculosis, and the incidence of positive reactions to the Mantoux tests in this group was 25 per cent, a proportion significantly higher than that of the control group and suggestive of the importance of the contact. In fact, a glance down the column headed Positive Mantoux Reaction, White, reveals that there was a significantly high rate of reaction in every family group, although in some the small number of cases forbids conclusions. The table further indicates that for every relationship, and in each race, the rate of positive responses to any test was always higher when the infected relative had died of tuberculosis than when the relative was merely ill with it. This difference is so consistent that the conclusion that there is some special significance in it is inescapable. I am inclined to conclude from this that a relative's dying of tuberculosis in a home is a serious hygienic hazard to the children in that home.

The data in the table suggest also that tuberculous parents are somewhat more of a menace to health than tuberculous siblings and that a tuberculous boarder may constitute a real threat to the child's health.

CONCLUSIONS AND SUMMARIES

A review of the responses to cutaneous tests and the family histories of 1,207 children from families containing tuberculous members has been reported.

The Pirquet test appears to be less sensitive than the Mantoux test and less likely to cause a false positive reaction; but there is a small but definite possibility of the Pirquet test causing a spurious negative reaction.

Roentgen and clinical examination of the chest is of little value in the diagnosis of tuberculosis of the childhood type.

The Loewenstein test, which is carried out by inunction using tuberculin in a glycerin extract, is described.

The Loewenstein test is less sensitive than either the Mantoux or the Pirquet test; when the reaction to a Loewenstein test is positive the reaction to the other cutaneous tests will almost certainly be positive.

A positive reaction to the Loewenstein test is a convenient criterion of the need for care in a sanatorium. The high incidence of positive reactions to the Mantoux and Pirquet tests makes them of little value in segregating the group needing care in a sanatorium, but the lower incidence of positive reactions to the Loewenstein test makes it useful for this purpose.

Children exposed to tuberculosis at home are more likely to have tuberculosis of the childhood type than are unexposed children.

A child from a home in which a member has died of tuberculosis is subjected to a greater risk of contracting the disease than one from a home in which a relative is ill with tuberculosis.

Boarders and lodgers with tuberculosis constitute a real menace to the health of children in that home.

A tuberculous parent is a greater hazard to the health of a child than a tuberculous sibling.

THE ICTERUS INDEX IN THE NEW-BORN INFANT

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Development of relatively accurate methods for the quantitative determination of the bilirubin content of the blood serum has led to acceptance of an icterus index of from 4 to 6 as normal for the adult. Latent jaundice is said to be present up to an index of 15, at which point clinical manifestations of jaundice appear. The need for several cubic centimeters of blood to perform these tests necessitates venipuncture, a requirement acting somewhat as a deterrent in determining the icterus index in infants and probably accounting for the dearth of routine studies of the bilirubin content of the neonatal blood serum. The method devised by Davis [1] for the use of small amounts of blood, if practical, would offer a simple way of doing this. Briefly, it consists of drawing into a capillary tube a few drops of blood obtained by puncture of the skin. The serum is separated by centrifugation and compared with known standards contained in tubes of the same bore. A serum matching a 1 : 10,000 solution of potassium bichromate represents an icterus index of 1, and a serum matching a 2 : 10,000 dilution, an index of 2. The standards continue in this manner up to 100 : 10,000, which represents an index of 100.

The capillary method is subject to the errors found in the more precise colorimetric tests, since none of them discriminate between bile pigments, the related hemoglobin derivatives (hematin) and the lipochromes (xanthophylls and carotenes), which may cause pseudo-icteric manifestations in both the skin and the blood serum. In the new-born child the carotenes may be ignored, and the error due to other lipochromes may be removed largely by obtaining the blood just before nursing time. Hemolysis is the most bothersome factor. To some extent it may be reduced by refraining from squeezing blood from the site of the puncture, by cooling and testing it immediately and by thorough cleansing of glassware. Other factors involved in hemolysis of the neonatal blood will be discussed later.

From the Newborn Department of the Holy Cross Hospital.

1. Davis, D.: Determination of Icterus Index with Capillary Blood, Am. J. M. Sc. **172**:848 (Dec.) 1926.

NEONATAL HYPERBILIRUBINEMIA

Using one or more of the several methods devised for determining the bilirubin content of the blood serum, numerous investigators [2] demonstrated, mostly by single tests, the presence of hyperbilirubinemia during the first week of life, the degree corresponding somewhat to the severity of the clinical jaundice. Similarly a moderate increase of the bile pigment content of the blood of the umbilical cord has been found.

A few observers have used the capillary method for determining the bile index in small series of cases. Thus Taylor [3] in 10 infants between the ages of 2 and 10 days found a bile index always above 20 whether or not clinical jaundice was present. Goldbloom and Gottlieb [4] showed that in 21 infants the index varied between 7 and 28 in the first week of life and that when jaundice appeared it remained higher when the infant was 10 days old than at birth. In infants without jaundice the index receded to nearly normal (from 5 to 7) at the end of the week. Snelling,[5] using this method to determine the daily icterus index of 20 infants, obtained higher readings but in general corroborated the observations of the other workers. Such findings indicate the presence of latent jaundice at birth and during the early days of life, even if icterus cannot be detected clinically.

RESULTS OF DAILY DETERMINATIONS OF THE ICTERUS INDEX ON ONE HUNDRED AND FOUR NEW-BORN INFANTS

During the course of a detailed investigation of a large number of newly born infants daily determinations of the icterus index were desired. The number of estimations required led to adoption of the Davis capillary method, which some had found to give fairly satisfactory results. Owing to the nature of the study only a small number

2. (*a*) Yppö, A.: Icterus Neonatorum and Bile Secretion in the Fetus and Newborn, Ztschr. f. Kinderh. **9**:208, 1913. (*b*) Hirsch, Ada: Physiologic Icterus of the Newborn, ibid. **9**:196, 1913. (*c*) Bang, F.: Icterus Neonatorum, Hospitalstid. **8**:637 (June) 1915. (*d*) Hallez, C. L.: Icterus in the Newborn, Nourrisson **13**:297 (Sept.) 1925. (*e*) Schiff, E., and Faerber, E.: Jaundice in the Newborn, Jahrb. f. Kinderh. **97**:245 (March) 1922. (*f*) Lucas, W. P.; Dearing, B. F.; Hoobler, H. R.; Cox, A.; Jones, M. R., and Smyth, F. S.: Blood Studies in the New-Born, Am. J. Dis. Child. **22**:525 (Dec.) 1921. (*g*) Mitchell, J. M.: Rôle of Hemolysis in Jaundice of the New-Born Infant, Am. J. Dis. Child. **36**:486 (Sept.) 1928; **38**:518 (Sept.) 1929. (*h*) Lereboullet, P.; Gournay, F. J., and Detrois: Recherches sur le sang et les urines dans l'ictère physiologique du nouveau-né, Nourrisson **19**:356 (Nov.) 1931. (*i*) Gordon, M. B., and Kemelhor, M. C.: Icterus Neonatorum, J. Pediat. **2**:685 (June) 1933.

3. Taylor, R.: The Icterus Index in Children, Am. J. Dis. Child. **34**:989 (Dec.) 1927.

4. Goldbloom, A., and Gottlieb, R.: Icterus Neonatorum, Am. J. Dis. Child. **38**:57 (July) 1929.

5. Snelling, C. E.: Icterus Neonatorum, J. Pediat. **2**:399 (April) 1933.

of infants could be observed at one time, so selection of subjects at random was necessary. No effort was made to choose subjects. The same personnel was used during the study, and each worker pursued the same observations throughout.

A total of 1,265 determinations of the icterus index were made on the blood of the cord and of the infants during the first twelve days of life. Blood counts and estimations of hemoglobin by the Dare method were made on 47 of these infants on the third, sixth and ninth days, respectively, and the coagulation and bleeding times were determined by the capillary tube method on the blood of 51 infants.

Of the 107 infants comprising the study, 3 were born with unmistakable jaundice. Since the object was to obtain the normal icterus curve through the first twelve days of life and since the birth of jaundiced infants could not be considered other than most unusual, the records of these infants have been omitted from those for the principal group. Their record will be considered separately. This, then, reduced the group observed to 104 infants.

MEAN DAILY ICTERUS INDEX

The mean icterus indexes of both the blood of the umbilical cord and the blood of the infants shortly after birth were about twice the normal adult index and were nearly identical, 12 and 13, respectively (table 1). Latent jaundice, therefore, was present at birth. After birth

TABLE 1.—*Icterus Index in Relation to Clinical Icterus in New-Born Infants*

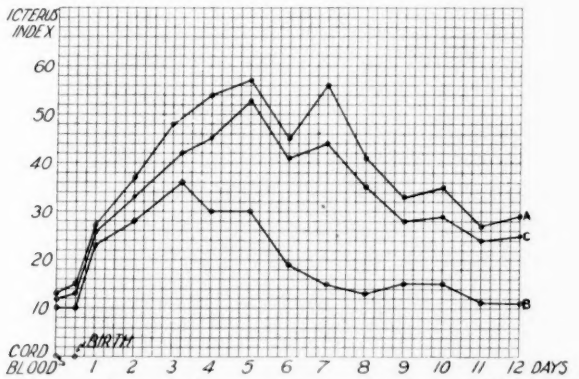
	Blood of Cord	Days												Average	Average Weight at Birth, Gm.	Average Loss of Weight, Gm.
		0	1	2	3	4	5	6	7	8	9	10	11	12			
Mean icterus index...	12	13	26	33	42	45	53	41	44	35	28	29	24	25	32	3,640	324
Infants with jaundice	..	..	0	8	38	45	63	56	47	36	26	15	8	9	..	.....	...

the mean daily index rose rapidly, reaching a peak (53) on the fifth day, after which there was a gradual drop to the twelfth day (25), at which point the index was twice the level found at birth and only slightly lower than the level of the first day (chart). In no case was the icterus index normal throughout the course of study. The record for clinical icterus in general followed the same trend. The total mean index for all the infants was 32.

ICTERUS INDEX FOR ICTERIC AND NONICTERIC INFANTS

Thirty-two (30 per cent) of the 104 infants manifested no clinical jaundice throughout the period of study. The bile index of this group

at birth was twice the adult normal (table 2), and after reaching a peak (36) on the third day it receded to the level at birth on the twelfth day (chart). The 72 (70 per cent) infants showing jaundice at some time had a considerably higher mean icterus index, which reached the peak (57) on the fifth day and declined slowly to the twelfth day, remaining at twice the level obtained at birth. Hyperbilirubinemia, therefore, prevails in the first twelve days of life whether or not jaundice is present. For the jaundiced group the mean index was slightly higher at birth and continued to a higher peak, which was reached two



Icterus index for infants during the first twelve days of life. A indicates the number of infants with jaundice; B, the number without jaundice; C, the average.

TABLE 2.—*Icterus Index in Icteric and Nonicteric Groups of New-Born Infants*

	Blood of Cord	Days													Average	Average Weight at Birth, Gm.	Average Loss of Weight, Gm.
		0	1	2	3	4	5	6	7	8	9	10	11	12			
72 icteric infants.....	13	15	27	37	48	54	57	45	56	41	33	35	27	31	37	3,568	336
32 nonicteric infants	10	10	23	28	36	30	30	19	15	13	15	15	11	11	19	3,712	302

days later than that for the group without jaundice. When the infants were 12 days old, the mean index was still twice the level found at birth and nearly three times that for the group without jaundice on the twelfth day. The height of the bile index generally corresponded to the severity of clinical jaundice, but this was not always the case. Thus, in several instances a bile index of 30 and occasionally even one of 60 was obtained when jaundice was not recorded at any time during the study. This paradox may be attributed to the tendency for jaundice to be masked by the ruddy color of the skin of the new-born child. When the scleras are yellow, jaundiced skin usually can be detected. The level of the bile index did not always parallel the severity of clinical

icterus. In a few infants with 2 plus readings for clinical icterus, the bile index was only 30. The total mean index for the icteric group was 37, as compared with 19 for the nonicteric group.

RELATIONSHIP OF CERTAIN FACTORS TO HYPERBILIRUBINEMIA

Sex.—Analysis of the data for the 55 boys and 49 girls revealed no relationship between sex and the icterus index, except possibly a slight difference that might be attributed to the influence of weight.

Weight.—The average icterus index for infants of low weight at birth was only slightly higher than that for infants of normal weight at birth, but in the overweight group the index was unusually low. The group with jaundice, with its high bile index, had an average birth weight lower by 144 Gm. than the group without jaundice (table 2). The initial loss in weight reached its height on the same day as the bile index, indicating that to some extent bilirubinemia was increased by the blood concentration occurring at this period. This could be but a minor factor, however, since the loss in weight of the icteric group was only 34 Gm. greater than that of the nonicteric group. Comparison of the weight at birth and loss in weight between the groups with indexes above and below average revealed little difference in the weight at birth and only a 31 Gm. greater loss in the group with indexes above normal.

Blood Constituents.—No relationship could be established between the bile index and the coagulation and bleeding times in infants with or without jaundice or those with decreased or prolonged coagulation and bleeding times. There was little change in the hemoglobin or erythrocyte level on the third, sixth and ninth days, the period when a rapid rise and fall of the icterus index occurred. These findings, as Snelling [5] has pointed out, indicate that icterus neonatorum probably is more than a simple hematogenous phenomenon based solely on destruction of blood in the early days. In the group with jaundice the hemoglobin content dropped 10 per cent from the third to the ninth day. No drop was observed in the group without jaundice. The bile index of infants with high hemoglobin readings on the third day was lower (9 per cent) than that of infants with low readings. However, the differences noted might be considered within the limit of error. In the group with high erythrocyte counts on the third day the icterus index was 12 points lower than it was in the group with low counts. This served to indicate further that destruction of blood was not the only factor involved in the development of icterus neonatorum. The findings recorded parallel closely those of Lucas,[2f] Mitchell [6] and Snelling.[5]

6. Mitchell, I. K.: Relationship of Jaundice and Weight to Blood Values in the New-Born Infant, Am. J. Dis. Child. **38**:518 (Sept.) 1929.

Prematurity.—Since only 3 infants in the series were premature, the relationship between the icterus index and prematurity could not be determined. Of these 3 infants, the one with the highest average index (62) was only two weeks premature. For an infant four weeks premature the index was 29, and for one three weeks premature it was 10. The latter showed no clinical jaundice.

Obstetric Data.—The icterus index was uninfluenced by the duration of labor. In fact, the average index in cases of labor lasting between six and eighteen hours was slightly greater than that in cases with a duration of labor at either extreme. Furthermore, no relationship could be detected between the mode of delivery and the height of the icterus index. Thus, the average bile index for the spontaneously (87 per cent) and operatively (13 per cent) delivered infants was identical.

TABLE 3.—*Hemolysis of Blood in Icteric and Nonicteric Infants*

	Blood in Cord	Days												Average	Average Weight at Birth, Gm.	Average Loss of Weight, Gm.
		0	1	2	3	4	5	6	7	8	9	10	11	12		
Percentage of hemolysis in entire group	38	31	69	51	46	42	40	42	56	44	41	40	42	49	45	3,640	319
Percentage of hemolysis in nonicteric group	43	34	86	64	62	59	70	57	50	57	45	50	61	64	57	3,712	302
Percentage of hemolysis in icteric group	31	32	65	49	39	37	29	35	57	40	40	38	36	45	39	3,586	336

HEMOLYSIS

Regardless of the care in obtaining and handling neonatal blood, it has been the experience of many that hemolysis occurs frequently. Taylor [3] found it present in nearly half of his specimens. The inherent tendency for neonatal blood to hemolyze has been attributed to many factors, such as interagglutination, hemolysis, isolysis, action of bacterial toxins and fragility of the red cells, but so far the exact nature of the hemolytic agent is not known. The same may be said of its source, whether or not it is of maternal, fetal or placental origin.

My experiences in respect to hemolysis have been much the same as those of others. In spite of meticulous care in obtaining, cooling and handling specimens, in cleansing glassware thoroughly and in making determinations promptly, 44 per cent of the samples showed some degree of hemolysis (table 3). The percentage was least in the blood of the cord and in the neonatal blood at birth and greatest in the blood taken at the end of the first day.

The average percentage of hemolysis in the nonicteric group was 57, as compared with an average percentage of 39 for the icteric group, a

difference of 18. Hemolysis was particularly uncommon in infants with a high bile index.

The blood of some infants hemolyzed more consistently than that of others. On analysis it was found that the average bile index for the groups in which hemolysis was common was 19, much lower than the general average. These observations, which indicate that the bile salts do not play an important part in causing hemolysis, are interesting in that they serve to corroborate in another way the laboratory experiments of Sanford and his associates,[7] who demonstrated a relatively high protective power of the blood serum of the normal new-born child against production of hemolysis by bile salts. The average weight at birth of the group in which hemolysis occurred frequently was considerably above the average (140 Gm.). No relationship could be established between loss in weight and hemolysis. The blood of girls hemolyzed more often than that of boys. At first this would appear to be a discrepancy, since the average weight at birth of girls was 183 Gm. lower than that of boys, but this could be explained by the fact that the girls whose blood hemolyzed most frequently were individually considerably overweight.

Hemolysis did not seem to be related to variations in the erythrocyte count, in the coagulation and bleeding time or in the hemoglobin content of the blood. The duration of labor or the mode of delivery did not play a part in the production of hemolysis; in fact, it occurred in a greater percentage of infants born of spontaneous labors and of labors of normal duration.

JAUNDICE AT BIRTH

Icterus neonatorum usually makes its appearance after the second day, but of the group of infants under observation 3 were born jaundiced. This is sufficiently remarkable in a series of this size to warrant brief mention.

The icterus index of all of these infants was high (table 4), and a rapidly progressive form of hemolytic anemia developed in all. Splenomegaly was absent. For the 2 who died, the values for hemoglobin and erythrocytes on the day of death were: (case 1) hemoglobin 16 per cent (Dare) and erythrocytes 910,000 per cubic millimeter; (case 3) hemoglobin 20 per cent and erythrocytes 1,000,000 per cubic millimeter. In 1 patient (case 1) the jaundice decreased toward the end. Two other children in this family had died of jaundice in the first week of life, and 1 was living at the age of 4 years. An autopsy performed on 1

7. Sanford, H. N.; Crane, M. N., and Leslie, E. I.: Bile Salt Hemolysis in New-Born Infants and Its Inhibition by the Blood Serum, Am. J. Dis. Child. **40:** 1039 (Nov.) 1930.

infant (case 3) revealed no evidence of anatomic obstruction of the bile tract or of hepatitis, and from the symptoms the possibility of obstructive jaundice was excluded. All 3 were born spontaneously at term.

SUMMARY

The need for several cubic centimeters of blood for determining the bilirubin content of blood serum has acted as a deterrent in making daily estimations as a routine on large series of new-born infants by standard methods. The Davis capillary method, requiring small amounts of blood, was used to determine the daily bile index of the blood of 104 infants during the first twelve days of life. A daily icterus index curve was established, which showed that latent jaundice is not only a neonatal but a late fetal characteristic. The bilirubin levels of the blood of the umbilical cord and the blood of infants at birth were nearly identical and twice the normal value for adults. The index rose during

TABLE 4.—*Record of Three Infants Born with Jaundice*

No.	Name	Sex		Blood of Cord	Days 0	1	2	3	4	5	6	7	8	9	10	11	Weight at Birth, Gm.
1	Jensen	M	Icteric index...	20	H	30	60	85	H	60	30	20	30	35*	...	...	3,300
			Clinical icterus	..	2+	2+	2+	2+	2+	+	+	+	+	0	...	...	.....
2	Coupland	M	Icteric index...	H	80	100	100	100	100	100	100	100	100	100	100	100	3,000
			Clinical index..	..	2+	4+	4+	4+	4+	4+	4+	4+	4+	4+	4+	4+	.....
3	Parry	F	Icteric index...	..	...	70	100	100	100	100	100*	...	...	...	...	...	3,060
			Clinical index..	..	+	4+	4+	4+	4+	4+	4+	...	...	...	...	...	.....

* Patient died.
H indicates hemolysis.

the first five days to 53, after which there was a gradual decline, so that by the twelfth day it was twice the level found at birth. Clinical icterus followed essentially the same trend, but while jaundice could not be detected in 30 per cent the bile index showed that hyperbilirubinemia prevailed in all. The average index for the group without jaundice was decidedly lower than that for the group with jaundice and the peak was reached on the third day, after which it receded, reaching the level at birth by the twelfth day. In the icteric group a higher peak was reached on the fifth day, and at the end of twelve days the index was still twice the level at birth. Possibly owing to peculiarities of the skin at this age, jaundice could not be detected definitely until the bile index was close to 30. Occasionally jaundice was not noticed when the index was 60. The icterus index was uninfluenced by sex, loss in weight, coagulation or bleeding time, duration of labor or type of delivery. It was unusually low in the overweight group but only slightly higher in the underweight group. The average weight at birth of the group with jaundice with a high bile index was considerably lower than that

of the group without jaundice. The hemoglobin and erythrocyte levels dropped only slightly over the course of nine days, and while the bile index for the group with high initial erythrocyte counts was lower than in the group with low initial counts, the difference was not great. Such findings indicate that possibly destruction of blood is not the only factor in causing hyperbilirubinemia in new-born infants. The fact that hemolysis occurred in 44 per cent of the samples of blood in spite of attempts to prevent this by careful technic points to the presence in the neonatal blood of some inherent hemolytic factor so far unrecognized. Hemolysis was least frequent at birth and most frequent at the end of the first day. Samples of blood with high indexes did not hemolyze as readily as those with low indexes, an observation indicating that the bile salts do not cause hemolysis but rather protect against it. Records of 3 infants omitted from the main group because they were born jaundiced are included. All had high bile indexes with nonobstructive jaundice, and in 2 fatal hemolytic anemia developed.

CONCLUSIONS

The capillary method is satisfactory for routine determinations of the icterus index of the blood of new-born infants.

Hyperbilirubinemia exists at birth and continues through the first twelve days of life regardless of the presence of clinical jaundice, which may not be detected until the index is close to 30.

The icterus index is uninfluenced by sex, loss in weight, coagulation or bleeding time, duration of labor or type of delivery. Low indexes are found in infants weighing above normal at birth, with no jaundice and a high hemoglobin or erythrocyte level.

Certain observations indicate that possibly destruction of blood is not the sole factor in producing neonatal hyperbilirubinemia.

The inherent tendency for the blood of new-born infants to hemolyze is not due to the presence of bile salts. They tend to protect against it.

A brief record of 3 infants born with jaundice is appended.

9 Exchange Place.

PREVENTION OF RICKETS WITH A COD LIVER OIL CONCENTRATE IN MILK

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This report concerns the use of cod liver oil concentrate containing vitamins A and D incorporated in a standard evaporated whole milk in the prevention of rickets. It also includes a study of the prevention of scurvy in the same infants by the use of canned ripe pineapple juice as the sole source of vitamin C.

The literature on the use of antirachitic agents incorporated in milk deals only with vitamin D added in various ways. It does not seem necessary to review these reports. The interrelationship of vitamins A and D in the prevention of rickets has been stressed by several investigators.[1] There seems to be no doubt that cod liver oil or some preparation of cod liver oil which includes both vitamins is the most reliable antirachitic agent available today for the prevention or the treatment of rickets. No clinical study has been reported on the amount of ripe pineapple juice necessary to prevent scurvy.

A group of twenty-six white infants was selected for this study on Jan. 17, 1934. These infants had been kept indoors in an institution, and no change was made in this routine except that they were kept outdoors, fully clothed, for occasional short periods during July, August and September. New infants are replacing those taken out of the institution, and the study is being continued. The series is not large, but the conditions under which the infants are kept is considered almost ideal, and this enhances the value of the results. The infants ranged in age from 2½ months to 14 months at the beginning of the study. They were well and healthy, and all but five were free from any signs of rickets or scurvy. Five infants had a few questionable clinical signs of rickets which are described.

This study was aided by a grant from the Page Milk Company, Merrill, Wis., which also supplied the milk used.

From St. Vincent's Infant Asylum and the Department of Pediatrics, Marquette University School of Medicine.

1. De Sanctis, A. G., and Craig, J. D.: A Five-Year Clinical Study of the Prophylactic Value of Antirachitic Agents, New York State J. Med. **34**:712 and 715, 1934.

P. G. (5 months of age) showed craniotabes, sweating of the head and slight thickening of the epiphyses on first examination, January 20. The calcium-phosphorus product, however, was 56 +, and the roentgenograms did not show the rickets.

G. K. (2½ months of age) had craniotabes on March 15. On April 20 she had craniotabes and beading of the ribs. On May 18 craniotabes was present only on the right side, and it had disappeared by June 21. Her calcium-phosphorus product on March 19 was 32.5, and on April 16, 40.4.

C. C. had healed rickets at 13 months of age, on January 20 (square head, prominent bosses, beading of the ribs, thickening of the epiphyses, flaring of the ribs and two teeth). His calcium-phosphorus product at the time was 57+.

J. R. (2½ months of age) on January 25 presented no signs of rickets. His calcium-phosphorus product was 48. On February 21 he had craniotabes, slight beading of the ribs and thickening of the epiphyses. The calcium-phosphorus product was 57+. The clinical findings persisted until June 21. In April two teeth erupted (4½ months of age).

R. S. (2½ months of age) had craniotabes on May 11. His calcium-phosphorus product was 62+. On June 21 the craniotabes was less marked, and it was absent on August 27.

J. H. had a calcium-phosphorus product of 28.9 on January 5 (5 months of age) but showed no clinical or roentgenographic evidences of rickets and has showed none thus far.

The cod liver oil concentrate used in the milk is a highly potent source of vitamins A and D obtained from the unsaponifiable fraction of cod liver oil. This concentrate, standardized for vitamin potency by biologic assays, was introduced into the standard evaporated milk during the evaporating process. The addition of 0.0444 Gm. of the concentrate to each 14½ ounce (429 cc.) can of evaporated milk enhanced its vitamin value by 2,000 units (U. S. P., revised 1934) of vitamin A and 400 units (U. S. P., revised 1934) of vitamin D. It is estimated that normal cow's milk contains from 900 to 1,800 units (U. S. P., revised 1934) of vitamin A per quart (946 cc.). Each lot of evaporated milk used was assayed according to a standard technic. The assays showed that each 14½ ounce can of evaporated milk contained 400 units (U. S. P., revised 1934) of vitamin D and not less than 3,200 units (U. S. P., revised 1934) of vitamin A. Each infant received from 8 to 16 ounces (from 240 to 480 cc.) of evaporated milk, diluted, per day. The taste, odor and appearance of the milk were not affected by the addition of the concentrate. The milk was similar in all respects, aside from its enhanced vitamin value, to a standard evaporated milk.

The vitamin C requirements of the infants were supplied with canned ripe pineapple juice. Each infant received from 1 (30 cc.) to 2 (60 cc.) ounces of juice per day.

Physical examinations were made at the beginning of the study and at monthly intervals, or more frequently, throughout the period of the study. One of us saw the infants almost every day. Roentgenograms of the radii and ulnas were made before the study was begun and at

TABLE 1.—*Average Amounts of Evaporated Milk Taken Daily by Each Infant*

	Age at Beginning, Months	Period of Study, Months	Gain in Weight		Gain in Length, Inches	Average Daily Intake of Evaporated Milk	
			Pounds	Ounces		Months	Ounces
D. M.	13	8½	7	10	3.6	1½	14
						3¾	11
						3¼	14
R. M.	13	8½	5	..	3.9	1½	14
						3¾	11
						3¼	14
K. K.	8	9⅓	7	..	4.4	2⅓	15
						3⅔	11
						3¼	13
R. B.	12	9⅓	4	4	3.4	2⅓	14
						3⅔	11
						3¼	14
P. G.	4⅓	11¾	10	3	5.2	2⅓	14
						3⅔	11
						5¾	15
B. L.	8½	9⅓	8	3	3.8	2⅓	14
						3⅔	11
						3¼	14
D. K.	8½	9¼	7	7	3.6	2⅓	14
						3⅔	11
						3¼	14
J. R.	2½	11¼	16	2	7.2	2¾	12
						5¼	15
						3¼	17
B. M.	8⅓	9¼	5	4	3.4	2⅓	15
						3⅔	11
						3¼	14
G. K.	2	7½	8	14	5.4	1⅔	10
						1¾	15
						1⅓	12
						2¼	20
M. L.	18	6½	6	6	1.5	3¼	11
						3¼	14
M. F.	2	10½	10	6	7.0	3¼	11
						2¼	13
						2	20
						3	15
J. L.	4	10½	12	8	7.5	3¾	13
						2¾	20
						1	15
						3	12
R. S.	3	9½	12	8	6.3	2¼	10
						3¼	18
						4	15
M. G.	5	5	2	12	1.3	2½	14
						2½	11
C. H.	13½	4	Lost	8	2.1	1½	15
						2½	11
L. D.	4½	4	2	8	1.6	4	14
C. C.	12	4	2	12	1.0	2½	15
						1½	12
C. P.	7⅔	5	4	3	3.0	5	13
L. N.	3	5	5	8	4.0	1	10
						1	14
						3	15
S. K.	5	4	5	2	2.5	4	15
J. S.	5	5	5	2	3.5	1	14
						4	15
M. W.	5	5	3	14	3.5	1	13
						½	14
						3½	15
A. S.	11	4	2	10	1.8	1	14
						3	15
J. H.	3	4	5	2	3.0	1	10
						1	13
						1	14
						1	15
J. W.	13½	4	2	14	0.8	3	14
						1	12

approximately monthly intervals thereafter. Determinations of the calcium and phosphorus of the serum were made before the study was begun and at monthly intervals thereafter.

The age (none of the children had been premature) and the gain in weight and in height of the infants from Jan. 17, 1934, to March 1, 1935, are listed in table 1. The average amounts of the evaporated milk taken daily by each infant are included in table 1. The erythrocyte counts and hemoglobin values for each child are listed in table 2. The results of the determinations of calcium and phosphorus are listed in table 3. The normal calcium-phosphorus product is considered to be 40 or over. During the period of study most of the infants had secondary hypochromic anemia. They were given various preparations of iron with a resulting rise in the hemoglobin content. It is known that secondary anemia is a factor in lowering the resistance to rickets.

SUMMARY

A group of twenty-six white infants was studied for periods of from four months (six infants) to thirteen and a half months (twenty infants). These infants were in the susceptible age periods for the development of rickets.

The sole source of vitamin D provided for these infants was a cod liver oil concentrate incorporated in a standard evaporated milk. Each infant received from 8 to 17 ounces of the evaporated milk per day, diluted with water according to the formula. This provided from 228 to 485 units of vitamin D (U. S. P., revised 1934).

The cod liver oil concentrate provided each infant with an additional supply of from 1,142 to 2,428 units of vitamin A. The milk was well taken and well tolerated.

The sole source of vitamin C for the infants was from 1 (up to 6 months of age) to 2 ounces of pineapple juice. The juice was well taken and well tolerated.

All of the infants made normal gains in weight and length during the period of study. No infant had any clinical, chemical or roentgenographic sign of rickets or of scurvy during this period. Five infants had some questionable clinical signs of rickets (one had a calcium-phosphorus product of 32.5), chiefly craniotabes, early in the period. There were no positive roentgenographic findings. The clinical and chemical findings became normal and remained so throughout the period (except for J. H.). One infant had clinical signs of healed rickets at the beginning of the period. His chemical and roentgenographic findings were normal and remained so throughout the period.

TABLE 2.—*Red Blood Cell Counts and Hemoglobin (Dare) in 1934 and 1935* *

	January, 1934		February, 1934		March, 1934		April, 1934		May, 1934		June, 1934		September, 1934		November, 1934		February, 1935	
	Hemoglobin	Red Blood Cells	Hemoglobin	Red Blood Cells	Hemoglobin	Red Blood Cells	Hemoglobin	Red Blood Cells	Hemoglobin	Red Blood Cells	Hemoglobin	Red Blood Cells	Hemoglobin	Red Blood Cells	Hemoglobin	Red Blood Cells	Hemoglobin	Red Blood Cells
B. L.	70	4.58	69	4.71	69	4.75	63	4.26	69	4.99	75	5.21	76	4.70	72	5.18	..	....
R. B.	80	4.52	80	4.80	70	4.51	75	4.76	75	4.57	75	4.62	78	4.67	75	4.75	..	....
D. K.	77	4.72	78	4.57	68	4.47	68	4.28	80	4.35	84	4.54	83	4.60	78	4.50	..	....
R. M.	69	4.42	75	4.31	66	4.55	78	4.97	73	4.73	81	5.22	75	4.62	78	4.66	..	....
J. R.	65	4.16	..	....	62	3.98	62	4.33	73	4.55	80	4.94	79	4.35	72	4.41	74	4.68
P. G.	65	4.56	68	4.20	71	4.70	65	4.53	70	4.82	75	4.67	69	4.28	71	4.19	..	....
K. K.	58	4.50	..	....	59	4.32	62	4.30	70	4.93	63	5.00	75	4.38	64	4.07	..	....
D. M.	..	....	60	4.18	60	4.24	57	4.09	63	4.63	70	4.08	82	4.43	68	4.57	..	....
R. M.†	..	....	60	4.19	57	4.28	58	4.28	75	4.85	83	4.85	80	4.42	70	4.26	..	....
J. L.	..	....	..	....	..	....	65	3.66	60	4.03	73	4.66	70	4.43	69	4.22	61	4.23
M. L.	..	....	..	....	59	4.30	64	4.55	57	3.97	79	4.88	75	4.61	80	4.56	..	....
G. K.	..	....	..	....	60	3.61	58	3.90	64	4.15	77	4.15	70	4.20	74	4.18	..	....
L. D.	60	4.39	65	4.48	72	4.45	68	4.22	74	5.14	..	....	..	....	..	....	..	....
M. G.	65	4.31	67	4.64	71	4.39	68	4.56	73	4.86	80	4.77	..	....	..	....	..	....
C. C.	55	4.60	57	4.81	55	5.00	65	4.93	75	5.37	..	....	..	....	..	....	..	....
M. F.	..	....	..	....	..	....	76	3.98	67	3.73	78	4.05	69	3.75	80	4.39	66	4.30
C. H.	..	....	62	4.87	70	4.73	67	5.25	75	4.93	..	....	..	....	..	....	..	....
R. S.	..	....	..	....	..	....	..	....	61	3.71	77	4.77	67	4.85	71	4.98	65	4.87
C. P.	62	4.47	78	4.79	68	4.93	65	4.26	..	....	..	....	..	....	64	4.57	..	....
L. N.	..	....	..	....	..	....	..	....	.	....	..	....	..	....	89	4.28	72	4.76
S. K.	..	....	..	....	..	....	..	....	..	....	..	....	..	....	62	4.87	55	5.12
J. S.	..	....	..	....	..	....	..	....	.	....	..	....	..	....	66	4.22	58	4.09
M. W.	..	....	..	....	..	....	..	....	..	....	..	....	..	....	71	4.32	63	4.19
A. S.	..	....	..	....	..	....	..	....	..	....	..	....	..	....	59	4.53	66	5.30
J. H.	..	....	..	....	..	....	..	....	..	....	..	....	..	....	66	4.35	60	4.59
J. W.	75	4.68	82	4.75	74	4.40	73	4.83	83	4.70	..	....	..	....	..	....	..	....

* The values for hemoglobin are given in percentage and those for red blood cells in millions.
† Ronald M.

TABLE 3.—*Results of Determinations of Serum Calcium and Phosphorus (1934)* *

	Jan. 17		Feb. 19		March 19		April 16		May 14		June 12		Oct. 3		Nov. 8		Dec. 15		Jan. 15, 1935		Feb. 27, 1935	
	Ca.	P.	Ca.	P.	Ca.	P.	Ca.	P.	Ca.	P.	Ca.	P.	Ca.	P.	Ca.	P.	Ca.	P.	Ca.	P.	Ca.	P.
M. G.	9.85	5.30	11.65	5.25	10.30	4.93	9.41	3.60	10.60	5.63	10.93	5.75	.....	....	.....	....	.....	....	.....	....	.....	....
R. M.	9.40	6.35	10.30	5.20	9.18	4.26	10.09	4.32	10.40	5.59	11.02	4.83	11.45	4.23	8.26	4.91	.....	....	.....	....	.....	....
D. K.	10.08	5.59	10.75	5.30	9.86	4.15	10.60	4.01	10.90	5.68	10.40	5.35	11.66	4.10	10.16	4.89	.....	....	.....	....	.....	....
B. L.	9.96	5.75	9.63	5.71	10.04	3.92	10.53	3.85	10.30	5.14	11.32	5.10	10.60	3.94	9.14	4.62	.....	....	.....	....	.....	....
P. G.	9.20	6.15	11.85	5.08	9.43	5.94	10.54	5.10	10.53	6.04	11.00	6.75	10.39	3.45	9.74	4.56	1.027	4.60	11.22	4.89	.....	....
R. B.	9.04	6.15	10.53	5.05	9.06	5.01	9.19	3.78	11.20	5.32	11.30	5.90	10.82	4.87	10.18	4.58	.....	....	.....	....	.....	....
K. K.	9.38	6.65	9.65	4.80	11.03	4.72	10.01	4.81	10.87	5.73	10.72	5.25	10.02	3.98	10.60	3.85	.....	....	.....	....	.....	....
J. R.	7.62	6.30	10.50	5.45	8.98	4.36	10.07	4.22	10.97	6.21	11.24	5.29	10.17	4.92	10.80	4.56	.....	....	11.54	4.98	11.02	4.78
C. C.	8.85	6.48	8.74	6.15	9.20	4.67	9.64	4.55	9.96	5.82	.....	....	.....	....	.....	....	.....	....	.....	....	.....	....
L. D.	8.65	5.80	10.07	4.05	10.01	4.08	10.28	4.15	10.86	6.54	.....	....	.....	....	.....	....	.....	....	.....	....	.....	....
D. M.	....	....	10.73	5.95	9.18	4.00	9.20	4.25	9.63	6.04	10.60	4.65	9.54	3.64	10.80	4.81	.....	....	.....	....	.....	....
R. M.†	....	....	9.85	6.75	10.53	5.20	9.42	5.50	10.93	5.35	10.82	5.70	12.08	3.92	8.28	4.43	.....	....	.....	....	.....	....
C. H.	....	....	8.52	5.00	9.20	5.68	9.18	4.40	10.30	5.97	11.41	4.15	.....	....	.....	....	.....	....	.....	....	.....	....
J. W.	8.13	6.25	10.74	5.02	9.41	4.67	9.64	2.70	.....	....	.....	....	.....	....	.....	....	.....	....	.....	....	.....	....
C. P.	9.07	6.14	9.63	5.22	10.05	5.11	11.42	4.18	.....	....	.....	....	.....	....	.....	....	.....	....	.....	....	.....	....
G. K.	....	....	.....	....	8.74	3.72	8.93	4.51	9.18	5.63	10.98	4.55	10.38	3.72	8.48	6.09	.....	....	.....	....	.....	....
R. S.	....	....	.....	....	.....	....	.....	....	9.27	6.68	11.80	5.38	9.54	3.47	10.32	5.55	9.86	5.20	10.22	4.78	10.86	4.64
M. F.	....	....	.....	....	.....	....	11.65	5.20	9.23	5.83	11.30	5.79	11.04	3.44	11.00	5.25	9.87	4.76	9.83	4.96	9.98	4.92
M. L.	....	....	.....	....	.....	....	9.42	4.19	9.67	5.87	11.24	5.36	11.06	3.67	8.98	....	.....	....	.....	....	.....	....
J. L.	....	....	.....	....	.....	....	9.63	4.23	10.53	6.08	10.92	5.32	10.62	3.56	11.41	3.95	10.23	4.88	10.96	5.22	10.20	4.84
L. N.	....	....	.....	....	.....	....	.....	....	.....	....	.....	....	10.81	3.71	8.86	5.55	10.40	4.96	9.68	5.02	10.72	4.96
S. K.	....	....	.....	....	.....	....	.....	....	.....	....	.....	....	.....	....	10.52	5.46	10.44	4.80	10.88	4.75	10.82	4.36
J. S.	....	....	.....	....	.....	....	.....	....	.....	....	.....	....	11.87	4.25	8.86	6.12	11.41	4.92	10.80	5.21	10.32	4.22
M. W.	....	....	.....	....	.....	....	.....	....	.....	....	.....	....	11.48	4.12	9.72	4.30	9.48	4.72	9.63	4.86	10.33	4.55
A. S.	....	....	.....	....	.....	....	.....	....	.....	....	.....	....	.....	....	9.10	5.02	9.70	5.12	8.62	5.25	9.78	5.24
J. H.	....	....	.....	....	.....	....	.....	....	.....	....	.....	....	.....	....	11.32	5.00	11.02	4.00	10.42	2.78	9.44	4.88

* The calcium content was determined by the methods of Kramer and Tisdall and of Clark and Collip; the phosphorus content, by the method of Youngburg and Youngburg (Phosphorus Metabolism, J. Lab. & Clin. Med. **16**: 158, 1930). All values are expressed in milligrams per hundred cubic centimeters.

† Ronald M.

CONCLUSIONS

It is evident that in this series of infants 228 units (U. S. P., revised 1934) of vitamin D daily in the form of cod liver oil concentrate in the milk provided adequate protection against rickets.

One ounce of ripe pineapple juice daily provided adequate protection against scurvy until the infants were 6 months of age. Two ounces was given after they were 6 months of age.

The routine administration of cod liver oil is greatly simplified by its inclusion in the milk.

ENTERITIS: ITS CONTROL AND PREVENTION BY THE DICK DIET KITCHEN AND NURSERY TECHNIC

LOUIS W. SAUER, M.D.
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Because of the likelihood of enteritis from cross-infection, Heubner,[1] in 1897, questioned the advisability of segregating sick infants in hospitals. To decrease the spread of enteritis in institutions for infants, he recommended a dual staff of nurses—"the one to care for the lower half of the infant; the other, to care for the upper half." Finkelstein [2] published an early paper on the prevalence of enteritis among bottle-fed infants. Nearly thirty years later, Czerny and Keller [3] said:

> On numerous occasions we have observed that asepsis and antisepsis failed to prevent the transmission of enteritis. With our increase in knowledge, however, house infections have decreased in frequency. In institutions where young infants are housed, it is, today, taken for granted that all food is sterilized, and kept so until it is consumed. When, in spite of precautions, enteritis breaks out, one must assume that the etiologic agent was transmitted during the care or feeding, probably by a carrier.

A search of the subsequent literature failed to reveal any specific technic aimed at the eradication of enteritis in institutions. The 1933 report of the League of Nations [4] showed that in every country many infants die from enteritis. In the continental registration area of the United States in 1932, 10,791 infants died of diarrhea and enteritis. With a total of over 120,000 deaths of infants a year, about 1 death in every 12 has been due to such infection.

For twelve years The Cradle of Evanston has functioned as a refuge for homeless infants until their legal adoption or rejection. Prevention of cross-infection has been the watchword of its nursing, medical and executive staffs. The adverse circumstances under which many illegitimate infants are born and the unhygienic environment of their neonatal period make many of them potential sources of infection of one kind or another. In the winter, they are not infrequently admitted with res-

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Read at a meeting of the Chicago Pediatric Society, Feb. 19, 1935.

1. Heubner, O.: Ueber Säuglingsernährung und Säuglingshospitäler, Berlin, A. Hirschwald, 1897.

2. Finkelstein, H.: Ztschr. f. Hyg. u. Infektionskr. **28**:125, 1898.

3. Czerny, A., and Keller, A.: Des Kindes Ernährung, Ernährungsstörungen und Ernährungstherapie, Vienna, Franz Deuticke, 1925, vol. 2, p. 200.

4. Diarrhea and Enteritis Deaths in the First Two Years of Life, Epidemiol. Rep., League of Nations, no. 166, March 1933, p. 115.

piratory infections; in the summer, with diarrhea. Observations at The Cradle in 1927 by the Dicks [5] led to the conclusion that it is more difficult to establish an aseptic technic in the nursery than it is to insure sterility of the feedings. The twelve years may be divided into two periods of six years each. During the former period (1923-1928) the diet kitchen and nursery technic [6] of a modern hospital for infants was followed; during the latter period (1929-1934), a diet kitchen and nursery technic evolved by Dr. Gladys Dick was rigidly adhered to. In the former period 942 infants were admitted; in the latter there were 1,650 admissions. The presence of enteritis from cross-infection during the former period and its absence during the latter period prove that the combined diet kitchen and nursery technic described here actually controls and prevents the spread of enteritis.

Of the 2,600 infants admitted since 1923, over 2,300 were legally adopted; 172 were returned to their mothers; 47, unfit for adoption, were transferred to other institutions, and 72 died during their stay at The Cradle—a mortality rate of 3 per cent of the admissions. Fifty-nine, or 82 per cent, of the deaths were due to enteritis. Forty of the infants apparently contracted the fatal infection more than two weeks after admission, i. e., two thirds of the fatal cases of enteritis resulted from cross-infection. For the first four years deaths due to enteritis averaged 4 per cent of the admissions; i. e., 1 of every 25 infants died of enteritis. Eighty-six of the 256 infants admitted in 1927 either had enteritis on admission or contracted it after admission. All of the 27 infants who died that year had enteritis; 21 of them contracted it after admission. During the six years that the individual aseptic nursery and diet kitchen technic perfected by Dr. Gladys Dick has been effective, 6 infants admitted with enteritis have died. In the six years no infant contracted enteritis after admission. In this period 0.3 per cent of the infants admitted died of enteritis.

The Dick technic is based on two essentials: sterility of the food and an individual, aseptic nursery technic which eliminates contamination of anything that enters an infant's mouth and nose. The infant remains

5. Dick, G. F., and Dick, G. H.: The Bacteriology of Dried, Powdered Milk Preparations Employed in Infant Feeding, Am. J. Dis. Child. **34**:1040 (Dec.) 1927. Dick, G. F.; Dick, G. H., and Williams, J. L.: The Etiology of Enteritis Associated with Mastoiditis in Infants, ibid. **35**:955 (June) 1928.

6. The first two weeks after arrival, the infant was kept in an isolated part of the institution, where a "special precautions" technic was rigidly followed. If apparently well at the end of that time, the infant was transferred to a crib in one of the rooms of the general nursery, where it remained, if well, until it left the institution. If the infant became ill in the interim, it would be sent to the "isolation" section or be transferred to a hospital. All foods, except protein milk, were sterilized by heat.

in the assigned crib until discharged. A unit of twelve cubicled cribs is supervised by a graduate nurse; the actual care of the infant (feeding, bathing, changing of diapers) is entrusted to pupil nurses, previously drilled in the technic. Everything within a cubicle is sterile or "clean" for the infant in the crib of that cubicle. Clean gowns and masks are put on by the physicians just before entering the nursery proper; when they enter a unit, hands (and the exposed parts of the forearm) are thoroughly lathered and scrubbed with a brush under warm, running water, soaked in basins of a solution of disinfectant and dried on clean towels. The stethoscope is cleaned in a solution of disinfectant after each use; tongue blades, applicators and specula are sterile. The hands are thoroughly cleansed (in the manner described) after an infant (or

Tabulation of the Deaths from Enteritis at The Cradle

Year	Admissions	Total Deaths	Total Deaths from Enteritis	Fatal Cases of Enteritis Contracted After Admission
1923	65	2	2	2
1924	83	6	5	4
1925	130	5	6	4
1926	157	7	5	1
1927	257	27	27	21
1928	250	8	8	8
6 year total	942	55	53	40
1929	254	5	5	0
1930	320	1	0	0
1931	271	3	0	0
1932	253	4	0	0
1933	272	3	1	0
1934	280	1	0	0
6 year total	1,650	17	6	0

any object in a cubicle) has been touched. At the feeding hour the "clean" supervising nurse wears a "clean" uniform and mask and sterile rubber gloves. She puts a sterile nipple on each infant's bottle and covers each nipple with a square of sterile gauze. The masked pupil nurse warms the bottle, puts on the cubicle gown, washes the hands as described, carefully removes the gauze and gives the feeding without touching the nipple or the upper part of the bottle before the feeding is completed. When a diaper is to be changed, the hands are washed and the cubicle gown is put on; after the diaper is changed, the hands are washed and soaked in a disinfectant just before and after the gown is removed. The diet kitchen is supervised by a graduate nurse who has no contact with the units of the nursery. She and her pupil nurse wear gown, cap and mask. Sterile rubber gloves are worn when removing sterile supplies from the autoclave. Feedings and drinking water are sterilized in pyrex nursing bottles in an autoclave at 15 pounds' pressure

for five minutes.[7] A minute perforation in the rubber cap of the bottle allows the air in the bottle to expand and contract. A gauze pad over the cap is secured by an elastic band before the bottle is placed in the autoclave. Feedings for a period of twenty-four hours are refrigerated until needed. Bacteriologic examination of such feedings showed the food to be sterile after a week at room temperature. This individual, aseptic nursery technic, in use for over six years, has furnished approximately sixty-six thousand days' care to 1,650 homeless infants without one instance of enteritis, impetigo or gonorrhea from cross-infection. During each of the last six years infants were admitted with these diseases, including 6 infants with fatal enteritis. Several of the latter group lived for weeks—ample time for cross-infection to have occurred had the technic not been flawless.

The only morbidity at The Cradle in the past six years was, as a rule, that with which an infant entered. Infants well on admission usually remained so until their discharge. The average stay has been shortened to forty days (an appreciable reduction); more infants occupied fewer cribs, and the nursing care was chiefly prophylactic. In 1931 an infant of 6 months was admitted a few days after the mother had died of scarlet fever. The infant had symptoms of a "cold." Within two weeks a pupil nurse caring for the infant contracted scarlet fever and the 4 other infants in the room, quite simultaneously, acquired "colds." Dr. Gladys Dick made cultures of material from the nose and throat for all of the infants and nurses of the unit. None of the infants' cultures showed scarlet fever streptococci, but the culture for 1 pupil nurse did. The unit was closed for a week, and everything in it was cleaned with a solution of disinfectant and autoclaved or painted before it was reopened. In January 1933 a nervous inadequately clad girl walked the streets with her 2 month old infant the night before she brought him to The Cradle. On entrance the infant had a temperature of 103 F.; bronchopneumonia was present. The infant made a complete recovery within six weeks, but 2 of the 4 infants in the room had colds within a week after the sick infant had been admitted. In January 1935 an infant of 6 weeks was admitted with symptoms of an acute cold (profuse rhinitis, fever, cough and sneezing). Within ten days, a premature infant in an adjoining cubicle, and soon afterward the four other infants in the other cubicles of the same room, acquired colds. None of the nurses on duty had colds during this period of time. The infants continued to gain in weight, and none had diarrhea or other complications. No infant in the other rooms of the unit, cared for by

7. Sauer, L.: A Simple, Inexpensive Stock Formula for Young Infants, J. Pediat. **1**:194 (Aug.) 1932; Enteritis in Infants: Prevention of Its Spread, ibid. **6**:753 (June) 1935.

the same nurses, contracted colds. These observations make it seem likely that the infective agent of these "colds" was air-borne and not transmitted by contact.

CONCLUSIONS

The Dick technic has furnished in six years a total of sixty-six thousands days' care to 1,650 homeless infants without any enteritis, impetigo or gonorrhea from cross-infection. This unique experiment brings concrete proof that sterile food, combined with an individual, aseptic nursery technic, when diligently pursued, will prevent the spread of these diseases. These observations should open a new era for infants in the care of institutions. There are many more potential foster parents than there are infants available for adoption. Most babies given up by their mothers are normal. Properly equipped institutions like The Cradle should house such infants until those fit are legally adopted. This field of pediatric endeavor warrants the interest and cooperation of physicians, for the technic described now offers a safe and humane solution for the care of most infants born out of wedlock.

DISCUSSION

DR. JOSEPH BRENNEMANN: I wish to congratulate Dr. Sauer and The Cradle on this excellent result.

One or two things interested me particularly. Is it permissible to inquire as to the cause of the extremely great mortality in 1927? Also, why were there eleven deaths from respiratory disease in the last four years, whereas there were only two in the four years preceding? Does the mortality include also that of those infants who were sent out of The Cradle and who may have died in the hospital to which they were sent?

DR. LOUIS W. SAUER: Dr. Gladys Dick has been much interested in this institution and has been a member of the board of directors since its inception. It seemed in 1927 that she had solved the problem of the high mortality when she found various kinds of micro-organisms in the powdered milks that were used there. That year, as I understand it, was a very bad year in a number of hospitals in Chicago. Many babies were admitted with enteritis due to the Morgan bacillus. The deaths in The Cradle in 1928 were due to cross-infection from infants who had this condition when they were admitted, due to slips in the nursing technic. One thing was found: The nurses before they went off duty made cotton swabs. Their hands were cleansed, but they were not sterilized, nor were the swabs sterilized. Eight deaths occurred, in spite of the fact that the food was absolutely sterile. Then it was found that the nursery technic was at least as important as the sterility of the food. The mortality reported includes that of all infants not legally adopted. Eighty-six infants in The Cradle had enteritis in 1927. This technic has solved the problem.

As to the question of cost, that is a matter of how one looks at it. In saving an infant's life no cost should be considered. The turnover that is possible without cross-infection is greater, and, on the whole, the average cost per infant per day in the institution is less than it was when so many had to stay longer because of acquired illness.

The cases in 1927 started in April and ended about November. There were then a few weeks without any cases, and there was another flareup in 1928.

The result achieved is unquestionably due to the combination of the absolutely sterile food and the technic of the nursing. It is a unique technic, but every step seems to be absolutely necessary. It may seem a great deal of trouble to autoclave the feedings of each infant each day, but every one is satisfied with the results.

STUDIES OF PHOSPHORUS OF BLOOD

IV. PHOSPHORUS PARTITION IN THE BLOOD OF CHILDREN WITH DISEASE

GENEVIEVE STEARNS, PH.D.
AND
EDNA WARWEG, M.S.
IOWA CITY

The normal variations in the components of blood phosphorus throughout the period of growth have been established in a previous study.[1] It has also been shown that both in severe rickets in rats [2] and in late rickets in children,[3] the ester (acid-soluble organic) phosphorus of the corpuscles as well as the inorganic phosphorus of the serum is much depleted and that during healing an increase in ester phosphorus is often the first alteration in the blood phosphorus with treatment. The phosphatase content is much increased during active rickets, and it decreases slowly with treatment.[3]

The following report concerns alterations in the blood phosphorus in diseases of infants and children, particularly such diseases as may be associated with alterations in serum calcium or inorganic phosphorus. The analytic methods used have been discussed in detail elsewhere.[1] Calcium was determined by the Kramer and Tisdall method; [4] the Fiske and Subbarow procedure [5] was used for final development of color in all determinations of phosphorus. Phosphatase was determined in plasma or in serum according to the technic of Kay [6] or of Jenner and Kay.[7] The Kay units have been multiplied by 50 in order to have the findings comparable.

In table 1 are listed the results of additional determinations of blood phosphorus in cases of infantile rickets, of tetany of infants under

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From the Department of Pediatrics, College of Medicine, State University of Iowa.

1. Stearns, G., and Warweg, E.: J. Biol. Chem. **102**:749, 1933.
2. Kay, H. D.: J. Biol. Chem. **99**:85, 1932.
3. (*a*) Stearns, G., and Warweg, E.: Studies of Phosphorus of Blood: III. The Phosphorus Partition in Whole Blood and in Serum and the Serum Calcium and Plasma Phosphatase During Healing of Late Rickets, Am. J. Dis. Child. **49**:79 (Jan.) 1935. (*b*) Smith, G., and Maizels, M.: Arch. Dis. Childhood **7**:149, 1933. (*c*) Smith, G.: ibid. **8**:215, 1933. (*d*) Bodansky, A., and Jaffe, H. L.: Phosphatase Studies, Arch. Int. Med. **54**:88 (July) 1934. (*e*) Kay, H. D.: ibid. J. Biol. Chem. **89**:249, 1930.
4. Kramer, B., and Tisdall, F. F.: J. Biol. Chem. **47**:475, 1921.
5. Fiske, C. H., and Subbarow, Y.: J. Biol. Chem. **66**:375, 1925.
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TABLE 1.—*Values for Calcium, Phosphorus and Phosphatase of Blood* in Children with Rickets, Tetany or Osteoporosis*

Name	Age	Diagnosis	Date	Serum Calcium, Mg. per 100 Cc.	Corpuscle Vol., per Cent	Whole Blood Phosphorus				Serum Phosphorus				Corpuscle Phosphorus		Plasma Phosphatase, Units
						Total	Lipoid	Ester	Inorganic	Total	Lipoid	Ester	Inorganic	Lipoid	Ester	
Average normal	0–2 mo.			11.3	30.1	37.2	10.5	21.3	5.3	14.9	7.7	0.5	**6.6**	17.0	69.8	23.0
H. L.	4 wk.	Tetany	4/10/33	6.5	36	42.9	10.7	20.8	**6.8**	....	..	...	**8.6**	....	(55.7)	39.0
			4/12/33	6.2	31	44.1	10.5	22.8	5.2	14.7	7.8	0.8	6.2	16.4	71.5	....
			4/24/33	8.9	25	38.0	10.7	21.3	4.9	16.8	10.0	0.9	5.8	12.8	83.6	31.5
			5/ 8/33	10.6	27	40.4	12.4	23.2	4.8	16.0	9.6	0.7	5.7	19.9	83.7	34.5
			7/20/33	11.3	36	40.0	11.7	24.1	4.3	14.6	8.2	0.9	5.3	....	65.2	33.1
J. M.	7 wk.	Tetany	5/23/34	7.8	23	36.6	9.8	**17.6**	**7.2**	15.8	7.6	0.3	7.5	17.4	75.5	76.6
			6/ 8/34	11.8	22	36.6	8.3	18.3	6.3	15.3	7.3	0.2	7.8	11.8	82.4	27.1
R. G.	2 mo.	Tetany	5/16/33	6.1	31	48.0	11.4	25.4	4.6	17.3	8.9	**2.1**	6.1	15.8	77.4	44.5
			5/27/33	7.6	29	41.4	10.5	23.1	6.2	....	...	...	...	....	....	39.4
Average normal	8–12 mo.			11.3	34.0	40.9	11.8	24.3	4.8	13.9	7.6	0.4	5.8	20.1	70.5	15.0
J. T.	8 mo.	Rickets, scurvy	8/23/34	9.6	30	35.8	12.6	**19.8**	2.7	**12.7**	8.1	**1.3**	**4.6**	23.0	63.0	7.9
			8/28/34	9.8	30	42.6	11.8	26.2	4.1	16.0	10.3	0.4	5.0	15.3	86.0	11.6
			9/ 4/34	10.3	..	....	....	....	...	....	...	...	6.0	....	....	....
J. Z.	9 mo.	Malnutrition	9/ 1/33	9.6	35	37.2	13.0	**19.5**	4.6	13.2	7.1	0.6	5.5	22.5	54.6	....
F. D.	12 mo.	Rickets	3/ 2/32	9.2	33	38.7	14.7	**20.4**	3.6	14.6	9.4	0.9	4.2	25.4	59.8	13.5
B. K.	19 mo.	Rickets (healing)	7/27/33	10.1	35	39.2	10.5	23.9	4.6	10.5	5.5	0.4	4.8	18.2	67.4	35.0
Average normal	2–3 yr.			11.3	35.0	43.0	12.7	26.0	4.4	15.6	9.6	0.6	5.2	18.5	73.1	9.5
D. R.	2 yr.	Osteoporosis, celiac disease	6/ 2/33	8.9	32	33.2	11.8	**18.9**	**2.5**	10.0	6.6	0.4	**3.0**	22.8	58.2	....
			7/ 1/33	12.6	32	46.5	11.8	28.9	5.3	16.3	8.4	0.7	7.3	19.0	88.8	13.5
E. M.	2 yr.	Celiac disease	4/27/32	10.9	25	34.8	10.1	**19.8**	4.5	11.7	6.6	0.2	5.1	**20.7**	78.2	8.5
Average normal	3–4 yr.			10.8	36.0	41.0	12.0	23.5	4.3	14.0	8.6	0.5	5.1	18.0	66.0	10.5
L. T.†	3 yr.		4/20/32	10.7	43	31.8	10.8	17.9	2.9	11.3	8.2	0.1	3.2	14.2	41.5	60.0
			4/24/32	6.6	46	38.1	13.7	21.3	3.1	13.3	9.4	0.3	3.5	18.9	46.2	70.0
			9/27/32	10.9	35	41.3	13.0	24.1	3.9	**16.0**	9.9	0.8	5.1	18.5	67.4	21.0
Average normal	4–6 yr.			10.7	37.0	40.6	12.7	23.5	4.2	15.1	9.0	0.7	5.5	18.9	62.4	11.0
L. S.	4 yr.	Rickets, diabetes insipidus	10/13/31	11.0	35	33.1	10.9	**19.1**	**2.9**	9.6	5.4	0.8	**3.5**	17.4	53.6	....
D. C.	5 yr.	Celiac disease	12/11/31	12.3	35	33.1	9.8	**20.0**	**3.1**	13.0	7.4	**.19**	**3.6**	11.4	53.2	....
Average normal	12–15 yr.			10.7	38.6	39.7	11.6	21.8	4.2	13.8	8.6	0.6	4.7	16.1	56.2	9.0
E. E.†	12 yr.	Rickets	1/20/33	10.7	43	33.8	11.0	**19.9**	**2.6**	12.0	8.0	0.8	**3.0**	15.2	**45.1**	71.5
			5/22/33	10.9	40	42.1	12.4	26.0	4.6	13.3	8.0	0.3	5.2	19.0	64.5	32.5

* Values for calcium and phosphorus are given in milligrams per hundred cubic centimeters; those for phosphatase, in units (Jenner & Kay). Values for phosphorus differing markedly from the normal are shown in bold face type.

† Values previously [3a] reported in detail.

2 months of age, of osteoporosis and of malnutrition. The data are arranged in order of increasing age, together with the average normal values for each age group, as previously determined.[1] For purposes of comparison, the first and last values for blood phosphorus of the two children with late rickets data for whom were previously reported [3a] have also been included in table 1.

The three young infants with tetany were treated only with vitamin D. The calcium content of the serum increased promptly with treatment, and the inorganic phosphorus content tended to decrease. The value for ester phosphorus of the corpuscles of the youngest infant, H. L., as estimated from the phosphorus content of whole blood, was low before treatment but increased to above normal as healing progressed. The ester phosphorus content of the corpuscles in the other two infants was increased at first observation. The ester phosphorus content of the serum of two of the three infants was also above normal levels. No significant alterations were observed in the lipoid fractions. The values for phosphatase for all of the infants were above normal and decreased with treatment. The findings for all three infants were considered typical of those observed in rickets. The age of the youngest infant (4 weeks) together with the findings we have reported gives additional support to the belief in the possibility of fetal rickets, even without the presence of noticeable osteomalacia in the mother.

Similarly, the values for phosphorus in the blood of the older infants and children with rickets showed alterations chiefly in the ester and inorganic fractions of phosphorus. The ester phosphorus content of the corpuscles tended to be low at the first observation, rising to above normal levels with treatment. The child with scurvy showed no increase in plasma phosphatase; Smith [3b] reported that in scurvy the phosphatase content is below normal; in rickets it is above normal. In this infant, the resultant of these two factors was apparently sufficient to keep the phosphatase within normal limits.

The children with osteoporosis due to malnutrition (celiac disease) or with malnutrition but no osteoporosis discernible by roentgen examination showed a decrease in ester phosphorus, both in the corpuscles and in the whole blood, together with the same tendency to overcompensation during the healing process that was observed during healing rickets, though to a less degree.

The values for phosphorus partition in the blood of seventeen children with osteomyelitis are shown in table 2. These children usually had some degree of secondary anemia. Three of them, P. J., R. C. and S. A., showed a marked degree of anemia. The ester phosphorus content of the corpuscles of all of these children was increased, as was observed previously in patients with secondary anemia.[8] The values for

8. Warweg, E., and Stearns, G.: J. Clin. Investigation **13**:411, 1934.

TABLE 2.—*Values for Calcium and Phosphorus* in Children with Osteomyelitis*

Name	Age, Years	Date	Serum Calcium, Mg. per 100 Cc.	Corpuscle Vol., per Cent	Whole Blood Phosphorus				Serum Phosphorus				Corpuscle Phosphorus		Comment
					Total	Lipoid	Ester	Inorganic	Total	Lipoid	Ester	Inorganic	Lipoid	Ester	
Normal 4–6 yr.			10.7	37.0	40.6	12.7	23.5	4.2	15.1	9.0	0.7	5.5	19.0	62.4	
P. J.	4	9/23/31	10.6	20	30.4	10.6	17.6	3.8	11.1	8.0	**1.6**	4.5	21.0	81.5	No operation
Normal 6–8 yr.			10.9	38.7	39.8	12.1	23.4	4.3	14.0	8.5	0.4	5.1	17.8	58.4	
S. C.	7	9/23/31	10.4	30	38.4	12.9	20.9	4.1	13.0	7.2	**1.25**	4.4	26.3	66.7	Orr drainage, 9/1/31
		11/ 5/31	10.8	38	34.0	11.8	19.3	3.6	12.5	7.2	**1.0**	4.3	19.2	**49.2**	Sequestration (?)
		12/11/31	10.4	34	31.3	10.7	18.0	**2.8**	11.5	7.2	**0.9**	**3.6**	17.6	51.2	Nearly healed
		2/16/32	10.6	38	39.6	9.8	25.7	3.9	....	...	...	...	....	....	Sequestrum
D. B.	7	10/27/31	11.9	37	36.9	12.6	20.4	3.6	13.3	7.8	**1.0**	4.4	20.8	**42.7**	No operation
		11/15/31	10.9	32	34.2	10.0	21.3	**2.9**	10.5	6.2	**1.0**	**3.6**	18.1	64.4	Drained
C. A.	7	10/28/31	11.3	..	....	....	....	...	13.5	7.1	**1.2**	5.1	....	....	Multiple lesion, draining
Normal 10–12 yr.			10.9	38.6	38.1	12.0	22.0	4.3	14.2	8.6	0.5	5.1	17.2	54.3	
J. M.	10	11/18/31	11.2	37	33.6	9.8	20.1	3.5	12.1	7.4	0.6	4.3	**13.8**	53.2	Untreated
R. A.	10	12/23/31	11.7	38	37.1	12.1	21.0	4.2	14.8	8.7	**1.0**	4.9	17.3	53.7	Untreated
G. S.	11	1/ 2/32	12.5	..	....	....	....	...	11.0	6.3	0.6	4.0	....	....	Untreated
H. G.	11	12/23/31	9.9	30	32.5	10.5	18.5	3.7	11.0	6.3	0.7	4.1	20.3	60	Drained, 12/21/31
Normal 12–15 yr.			10.7	39.7	38.6	11.6	22.7	4.2	13.8	8.6	0.6	4.7	16.1	56.6	
A. M.	13	9/11/31	10.9	34	36.2	12.4	20.8	**3.2**	12.0	7.6	**1.2**	3.3	**21.8**	58.8	Multiple old lesions
		12/19/31	11.0	37	36.4	12.4	20.0	3.8	12.3	7.4	0.5	4.4	**20.8**	53.2	Drained, 12/10/31
G. B.	13	10/ 5/31	11.2	41	33.8	10.7	19.7	3.2	13.1	8.3	**1.1**	3.8	14.1	**46.1**	Drained, 9/28/31
I. B.	13	12/30/31	11.9	36	43.0†	10.3	21.1	3.5	11.9	6.4	**0.9**	4.5	17.0	56.9	Multiple lesions
A. C.	13	1/23/32	11.8	36	36.1	10.6	21.3	4.1	15.0	9.6	0.4	5.0	**12.5**	58.0	Multiple lesions
		2/18/32	10.6	33	36.2	12.8	20.0	3.1	12.7	8.6	0.3	4.0‡	**21.2**	60.0	Drained; very ill
T. C.	14	10/28/31	10.6	..	....	....	....	...	12.5	7.5	**1.0**	3.9	....	....	Old, healed lesions; some exacerbation
		11/15/31	10.5	35	35.2	10.6	21.0	3.5	11.7	6.4	**1.0**	4.2	18.3	58.0	
L. S.	14	11/ 5/31	11.4	35	31.5	11.0	17.0	3.3	12.0	6.9	**0.7**	4.1	18.6	**47.1**	Two months after operation
R. C.	15	11/18/31	10.2	**28**	33.0	8.5	20.2	4.3	10.4	**4.8**	**1.0**	4.7	17.5	**69.6**	Badly infected tibia; drained, 11/10/31; other lesions not drained
E. B.	15	10/27/31	11.0	31	32.6	10.6	18.3	3.5	13.1	8.0	**0.9**	4.3	16.4	57.1	No operation
S. A.	16	8/26/31	**8.5**	**29**	36.4	12.5	20.2	3.5	17.4	10.7	**1.9**	4.9	17.0	**64.8**	Drained, 8/21/31
		10/24/31	9.7	..	....	....	....	...	12.3	7.0	**1.3**	4.0	....	....	

* Values for calcium and phosphorus are given in milligrams per hundred cubic centimeters. Values for phosphorus differing markedly from the normal are shown in bold face type.

† Undetermined phosphorus, 8.1 mg.

‡ Serum phosphatase, 23.0 units (normal for age).[7]

ester phosphorus of the corpuscles of four of the other children of this group were definitely low. This lowering of ester phosphorus apparently did not accompany any definite stage of the infection, for in some of the children the lesions were healing at the time of the lowest values while in the case of others the low values were observed before drainage. The values for lipoid phosphorus of the corpuscles of some of the children were also low, while those for others were increased. No consistent relationship was observed between the stage of the disease and the level of lipoid phosphorus in the corpuscles or in the serum. The most striking and consistent finding for the group was the marked increase in ester phosphorus of the serum, an increase noted in eighteen of the twenty-four reported values. The quantities observed were often more than double the normal. Only one determination of phosphatase was obtained from this group of tests. The patient on whom this determination was made showed massive destruction of bony tissue, and the value for phosphatase was definitely above normal. Of twelve values obtained from other patients with osteomyelitis, only three were above normal.

Table 3 reports the values observed for three children with hypercalcemia. The 2 year old child, J. A., died of mastoiditis. The postmortem examination showed complete absence of the thyroid gland; no enlarged parathyroids were noted. The inorganic phosphorus of the serum was much decreased, but the ester phosphorus content of the corpuscles was within normal limits. The ester phosphorus of the whole blood, owing to the presence of anemia, was lower than normal. Unfortunately, a determination of the ester phosphorus of the serum was not obtained at the time of the most severe anemia. Using the very high value for ester phosphorus of the serum obtained in the previous analysis, the ester phosphorus content of the corpuscles would be approximately 110 mg. Such markedly elevated values as these have been observed in adults with severe anemia,[8] likewise a decrease toward the normal, as in this child, occurred when the percentage of red cells increased. The values for phosphatase were lower than normal, as has been observed in cretinism.[3c]

The second child whose blood values are reported in table 2, G. W., had suffered a pathologic fracture of the hip. Because of the elevation of serum calcium the parathyroid region was explored. No enlarged parathyroid glands were found but two normal glands were removed on Nov. 4, 1931. The serum calcium remained high. The fracture of the bone healed very slowly, but subsequent inquiry indicated that the boy had since grown normally and had been without recurrence of pathologic fractures. The ester phosphorus content of the whole blood of this subject was about half the normal value at the time of first examination, and it rose but slowly, even though the child was given a diet rich in

TABLE 3.—*Values for Calcium, Phosphorus and Phosphatase of Blood in Children with Hypercalcemia* *

Name	Age, Years	Diagnosis	Date	Serum Calcium, Mg. per 100 Cc.	Corpuscle Vol., per Cent	Whole Blood Phosphorus				Serum Phosphorus				Corpuscle Phosphorus		Plasma Phosphatase, Units
						Total	Lipoid	Ester	Inorganic	Total	Lipoid	Ester	Inorganic	Lipoid	Ester	
Average normal 2-3 yr				11.3	35.0	43.0	12.7	26.0	4.4	15.6	9.6	0.6	5.2	18.5	73.0	9.5
J. A.	2	Cretinism	6/11/32	13.5	..	....	....	....	...	13.6	7.5	**3.1**	3.0	....	....	....
			6/15/32	12.1	**18**	40.4	12.2	**22.6**	**3.0**	....	...	...	3.5	....	(110)	....
			10/ 1/32	13.6	31	36.0	10.7	**22.1**	**2.9**	12.8	8.3	0.7	3.6	16.1	70.0	6.5
			11/ 3/32	15.9	30	35.5	**10.0**	**21.2**	4.4	13.7	7.6	**1.3**	**7.0**	15.6	68.0	7.5
Average normal 12-15 yr				10.7	39.7	38.6	11.6	22.7	4.2	13.8	8.6	0.6	4.7	16.1	56.6	9.0
G. W.	12	Pathologic fracture, hyperparathyroidism (?)	8/27/31	13.6	34	33.6	**20.4**	**11.0**	**2.4**	13.0	8.2	**1.9**	**2.8**	**44**	**25.0**	....
			10/24/31	15.0	35	32.6	13.0	**16.3**	**2.2**	13.3	8.8	**1.5**	**2.8**	22.2	44.0	....
			11/ 3/31	15.5	33	27.8	10.5	**14.8**	**2.6**	11.9	8.2	0.7	**2.8**	16.7	43.4	....
			11/ 6/31	15.0	..	....	....	....	...	11.4	8.0	0.3	**3.0**	....	....	....
J. W.	14	Hyperparathyroidism (?)	3/ 4/33	14.0	43	40.7	13.0	24.1	3.7	....	...	...	4.3	....	....	....

* Values for calcium and phosphorus are given in milligrams per hundred cubic centimeters; those for phosphatase, in units (Jenner & Kay). Values for phosphorus differing markedly from the normal are shown in bold face type.

calcium, phosphorus and vitamin D. The ester phosphorus content of the corpuscles was likewise very low, rising slowly. The degree of anemia was insufficient to account for the high value for lipoid phosphorus observed. The child's previous diet had been very poor; so the low values for ester phosphorus seemed probably due to poor nutrition rather than to the hypercalcemia.

The third patient with hypercalcemia showed no abnormalities of blood phosphorus. In general, the alterations of blood phosphorus in the hypercalcemic subjects seemed unrelated to the high values for calcium but dependent rather on accompanying malnutrition or anemia.

The values for blood phosphorus of sixteen children with renal disturbance together with the normal values for children of the same ages are listed in table 4. The values for serum calcium of four of the five children with nephrosis are somewhat below the usual levels for children. The lipoid phosphorus content of the serum of M. M. was nearly double the normal value, but none of the other children with nephrosis showed increase in lipoid phosphorus of either the serum or the corpuscles. The values for phosphorus for the other four children were approximately normal, and such shifts from the normal as were observed, for example, the lessened ester phosphorus content of the whole blood of R. O. and V. K., can be ascribed to the accompanying malnutrition. Similarly, in the children with acute hemorrhagic nephritis, none of whom had been ill very long, the values for blood phosphorus tended to be within the normal range. The exception here was the high value for total phosphorus observed for R. H. This child was the only one of this group showing a markedly increased value for nonprotein nitrogen, and the total phosphorus content of the whole blood was definitely above normal, the increase being distributed among all fractions.

The blood phosphorus of the children with the more chronic types of nephritis showed much greater variations from the normal, as has been observed by other investigators studying blood phosphorus in renal disease in adults.[9] These children were seriously ill. The values for blood were obtained from E. L. and V. K. (second value) the day preceding death and from F. M. and A. K. during the terminal stage of the disease. Three of the four children showed marked retention of nitrogen; two, at least, suffered from severe anemia, which in itself affects the levels of blood phosphorus. The number of determinations in the different types of chronic nephritis is insufficient to permit conclusions, except that retention of phosphorus in these patients is apparently not confined to the inorganic fraction, but increases may be observed also in each of the other components, and also the presence of unusual forms of phosphorus may be noted, as for V. H.

9. Byrom, F. B., and Kay, H. D.: Brit. J. Exper. Path. **8**:429, 1927. Greisheim, K., and Lucas, E.: Ztschr. f. klin. Med. **107**:172, 1928. Hoesch, K.: ibid. **121**:305, 1932.

TABLE 4.—*Values for Calcium, Phosphorus and Phosphatase* in Children with Nephritis or Nephrosis*

Name	Age, Years	Diagnosis	Date	Serum Calcium, Mg. per 100 Cc.	Corpuscle Vol., per Cent	Whole Blood Phosphorus				Serum Phosphorus				Corpuscle Phosphorus		Plasma Phosphatase, Units	Nonprotein Nitrogen	Serum Protein
						Total	Lipoid	Ester	Inorganic	Total	Lipoid	Ester	Inorganic	Lipoid	Ester			
Average normal	2–3			11.3	35	43.0	12.7	26.0	4.4	15.6	9.6	0.6	5.2	18.5	73.1	9.5	35.0	7.2
Average normal	4–6			10.7	37	40.6	12.7	23.5	4.2	15.1	9.0	0.7	5.5	18.9	62.4	11.0	35.0	7.2
Average normal	8–10			11.0	36	38.0	11.8	21.7	4.3	14.0	8.6	0.4	5.0	17.6	59.7	9.0	35.0	7.2
Average normal	11–15			10.7	40	38.6	11.6	22.7	4.2	13.8	8.6	0.6	4.7	16.1	56.6	6.5	35.0	7.2
D. G.	2½	Nephrosis	9/13/34	9.3	33	43.6	14.1	25.6	3.8	18.7	13.6	0.4	4.9	15.1	77.0	7.7	29.4	3.6
D. S.	8	Nephrosis	10/ 2/33	9.4	34	42.8	14.2	24.3	4.1	16.9	11.3	0.2	5.2	19.4	71.4	10.0	....	4.1
M. M.	9	Nephrosis	8/20/31	7.8	..	....	....	....	...	**25.8**	**17.5**	**3.9**	4.3	....	....	....	36.4	5.8
R. V.	10	Nephrosis	9/13/34	9.6	29	32.4	9.6	**18.3**	4.2	13.2	7.9	0.1	5.1	15.0	60.6	5.2	38.6	1.7
V. K.	13	Nephrosis	12/13/33	10.6	36	36.6	13.4	**19.7**	3.6	14.8	9.8	1.1	4.1	19.7	52.5	11.6	....	5.2
N. S.	3	Acute nephritis	10/11/33	10.1	33	38.8	11.2	23.1	4.3	15.1	9.3	0.7	4.9	15.1	68.5	7.5	54.5	6.8
R. H.	6	Hemorrhagic nephritis	7/26/33	....	..	**48.0**	14.3	26.6	5.6	....	....	...	...	....	....	....	89.0	5.7
S. S.	14	Hemorrhagic nephritis	4/ 7/34	11.6	33	39.0	10.7	24.0	4.1	12.4	7.0	0.2	4.9	18.2	66.4	....	52.2	...
K. C.	8	Chronic nephritis	7/29/31	9.0	..	**47.2**	**21.0**	22.8	3.8	**20.5**	8.9	**4.9**	**7.3**	....	....	....	67.3	...
M. B.	12	Diffuse nephritis	7/15/31	8.7	..	....	....	....	...	**21.5**	...	...	7.7	....	....	....	57.0	...
F. McC.	14	Diffuse nephritis	7/ 6/34	8.8	17	**31.4**	12.8	**13.5**	4.9	17.2	8.3	**3.6**	5.4	**34.6**	61.5	7.5	205.0	4.0
E. L.	4	Nephrosclerosis	10/25/33	8.6	10	**26.5**	12.9	**8.9**	4.8	16.3	10.9	0.3	5.5	31.0	86.0	14.3	240.0	7.0
			.....	....	..	....	....	....	...	....	....	...	...	....	....	....	.....	...
V. H.	11	Acute nephritis	2/ 8/34	....	28	56.4*	12.8	26.3	6.6	**19.8**	11.8	**1.1**	6.6	15.3	91.0	....	282.0	...
		Uremia	2/10/34	10.0	28	53.8*	14.9	22.1	6.5	**20.9**	13.2	**1.2**	6.7	19.3	75.5	....	300.0	...
A. K.	14	Pyonephritis	7/25/31	7.7	..	....	....	....	...	**35.8**	**19.1**	**4.5**	**10.9**	....	....	....	50.0‡	...

* Values for calcium and phosphorus are given in milligrams per hundred cubic centimeters; those for phosphatase, in units (Jenner & Kay). Values for phosphorus differing markedly from the normal are shown in bold face type.

† Undetermined phosphorus, 10.7 and 10.3 mg.

‡ Plasma nonprotein nitrogen.

Essentially normal quantity and distribution of blood phosphorus were observed in five children with markedly retarded growth, in two children with osteopsathyrosis and in three children under treatment for celiac disease. Examination of blood of four children after partial thyroidectomy showed no unusual findings in the blood phosphorus. The ester phosphorus content of the whole blood of seven diabetic children with blood sugar varying from 150 to 250 mg. per hundred cubic centimeters was somewhat decreased, varying from 18.1 to 21.8. The serum inorganic phosphorus varied from 3.3 to 4.8. Similar findings have been noted in adults with diabetes by Meier and Thoenes.[10]

In all of the children studied, malnutrition seemed to be accompanied by somewhat decreased or low normal values for ester phosphorus of the whole blood; similarly the inorganic phosphorus content of the serum was near the lower limit of normal. A prompt rise in these components was observed as the child's nutritional status improved. Only in the children with untreated celiac disease was the degree of malnutrition severe enough to cause marked changes in ester phosphorus.

SUMMARY

The phosphorus partition has been studied in whole blood and in serum of children with disease.

In three young infants with tetany, the findings were characteristic of rickets, i. e., a lowered value for ester phosphorus of the corpuscles and an increased value for phosphatase.

In children with osteoporosis (celiac) and with malnutrition, the ester phosphorus of the corpuscles was also definitely decreased, though not to the degree observed in rickets.

Children with osteomyelitis showed very high values for the ester phosphorus of the serum; the ester phosphorus of the corpuscle was often decreased. If the degree of anemia was marked, a tendency toward an increased amount of ester phosphorus in the corpuscles was observed.

In three children with hypercalcemia, no consistent alterations of the blood phosphorus were observed which could be ascribed to the hypercalcemia.

In children with renal disturbance, little change from the normal was observed until renal damage was severe. Then alterations in all forms of blood phosphorus were observed.

No outstanding alterations in the blood phosphorus were observed in children with dwarfism, hyperthyroidism, mild diabetes or osteopsathyrosis.

10. Meier, R., and Thoenes, E.: Deutsches Arch. f. klin. Med. **172**:160, 1931; Arch. f. exper. Path. u. Pharmakol. **161**:119, 1931.

TOXICITY OF ORGANS OF ANIMALS DYING AFTER INJECTION OF EMULSIONS OF STOOLS OF PATIENTS WITH POLIOMYELITIS

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The experiments reported here were performed to determine (1) the toxicity of the spinal cords of guinea-pigs dying after the injection of an emulsion made of stools obtained from patients with poliomyelitis, (2) the bacteriology of the emulsions made of the spinal cords of these guinea-pigs, (3) the relative toxicity of the various emulsions made of organs obtained from normal animals and of those given injections, and (4) the bacteriology of the emulsions made of the various organs.

TOXICITY OF THE CORDS

The spinal cord was taken from a guinea-pig weighing 250 Gm. The average weight of the cord from the laryngeal cartilage to the conus was approximately 0.5 Gm. In order to secure emulsions of the spinal cord for purposes of standardization, 0.5 Gm. of cord was ground in a mortar and then emulsified in 15 cc. of physiologic solution of sodium chloride, each cubic centimeter of which contained at least 0.03 Gm. of guinea-pig cord.

Emulsions were obtained of the cords of guinea-pigs that died after the subcutaneous injection of emulsions made of stools of patients with poliomyelitis. The emulsions were standardized in the same manner as the stools were in a previous [1] study and were injected subcutaneously into other guinea-pigs. A cystic lesion was always the result, and death occurred in 96 per cent of the animals (table 1). The dose that killed a guinea-pig weighing 250 Gm. within forty-eight hours after the injection ranged from 1 to 3 cc. The minimum lethal dose was never more than 3 cc., although it frequently was less.

Each emulsion made of the stool of a patient with poliomyelitis was injected into only one guinea-pig, so that the number of guinea-pigs used denotes the number of patients whose stools were used in the test. Injections of emulsions of the spinal cords of normal guinea-pigs and rabbits prepared and standardized in the same manner usually caused

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1. Toomey, John A.: Demonstration of a Toxic Factor in the Stools and Urines of Poliomyelitis Patients, J. Prev. Med. **6**:379, 1932.

nothing more than a fleeting induration and never death in the test animals (table 2). The animals into which were injected emulsions of the spinal cords of normal guinea-pigs or rabbits were not immunized, as

TABLE 1.—*Reactions of Guinea-Pigs to the Subcutaneous Injection of Emulsions Made of Spinal Cords of Guinea-Pigs That Died After the Injection of Emulsions of Stools or Urine of Patients with Poliomyelitis*

No. of Guinea-Pigs	Injection	Died, Hr.			Lesion		
		12	24	48	Inflammatory	Cystic	None
25	3 cc. of emulsion made of spinal cord and brain of guinea-pig that died of injection of an emulsion of stool of a patient with poliomyelitis	4	13	7	0	25	0
20	3 cc. of emulsion made of spinal cord and brain of normal guinea-pig	0	0	0	16	4	0

TABLE 2.—*Reactions of Rabbits to the Subcutaneous Injection of Emulsions of Spinal Cords of Normal Guinea-Pigs and Rabbits*

No. of Rabbits	Average Weight, Gm.	Injection	Died, Hr.			Lesion		
			12	24	48	Inflammatory	Cystic	None
4	525	6.3 cc. of emulsion of spinal cord of normal guinea-pig	0	0	0	0	0	4
2	492	5.9 cc. of emulsion of spinal cord of normal rabbit	0	0	0	1	0	1
2	500	7.2 cc. of emulsion of spinal cord of normal rabbit	0	0	0	2	0	0

TABLE 3.—*Reactions of Guinea-Pigs to the Subcutaneous Injection of Emulsions from the Spinal Cords of Guinea-Pigs Dying After the Injection of Emulsions of Stools of Patients with Poliomyelitis* *

No. of Guinea-Pigs	Injection	Died, Hr.			Lesion		
		12	24	48	Inflammatory	Cystic	None
20*	3 cc. of emulsion of spinal cord of animal that died after subcutaneous injection of emulsion of stool of patient with poliomyelitis	3	11	5	3	17	0

* These animals had previously received an injection of an emulsion of the brains and spinal cords of normal guinea-pigs.

shown by the fact that local cystic reactions and often death (95 per cent) were caused by subsequent injections of emulsions of the spinal cords of guinea-pigs that died after the injection of emulsions of stools of a patient with poliomyelitis (table 3).

Postmortem changes at normal temperature did not account for the toxicity of the emulsions of guinea-pig spinal cords, as emulsions made

of spinal cords of normal guinea-pigs kept for three days at a temperature of 37 C. and then injected into guinea-pigs caused no reaction (table 4).

The toxicity of emulsions of spinal cords was not enhanced by refrigeration, since emulsions of the spinal cords of guinea-pigs that died of injections of emulsions of stools of patients with poliomyelitis were equally potent whether they were obtained immediately or several days after death (table 5).

Emulsions were prepared of the spinal cords of guinea-pigs that died after the injection of emulsions of stools of patients with such

TABLE 4.—*Reactions of Guinea-Pigs to the Subcutaneous Injection of Emulsions Made of Cords of Normal Guinea-Pigs*

No. of Guinea-Pigs	Injection	Died, Hr.			Lesion		
		12	24	48	Inflammatory	Cystic	None
10	3 cc. of emulsion of spinal cord of normal guinea-pig*	0	0	0	2	0	8

* In this experiment the animal was killed and kept for 3 days at 37 C. before autopsy.

TABLE 5.—*Reactions of Guinea-Pigs to the Subcutaneous Injection of Emulsion of Spinal Cords* *

No. of Guinea-Pigs	Injection	Died, Hr.			Lesion		
		12	24	48	Inflammatory	Cystic	None
5	3 cc. of emulsion of cord obtained within 1 hr. after death of guinea-pig	1	3	1	0	5	0
5	3 cc. of emulsion of cord obtained 7 days after death of guinea-pig	0	4	1	0	5	0

* These emulsions were made of the cords of guinea-pigs that died after the injection of emulsions of stools of patients with poliomyelitis. On some of these animals the autopsy was performed immediately and on some, several days after death. The bodies were kept in the icebox during the interval between death and autopsy.

clinical conditions as enteritis, pneumonia, diphtheria and scarlet fever. Many of the guinea-pigs into which these mixtures were injected died (50 per cent; table 6).

The relative incidence of the number of deaths after the injection of emulsions of either stools or spinal cords did not constitute differentiating evidence, but in carrying the toxic factors in series by subsequent injections it was found that the spinal cords of guinea-pigs that died after the injection of emulsions of stools of patients with poliomyelitis were lethal to at least the fifteenth experimental generation. On the other hand, the spinal cord of not one of the guinea-pigs that died after the injection of emulsions made of stools from patients ill

with diseases other than poliomyelits was toxic after the third experimental generation (table 7).

The following method was used:

After the death of the guinea-pig into which was injected an emulsion of the stool of a patient with the clinical condition named, the spinal cord of the dead animal was made into an emulsion, which was injected into another guinea-pig. In turn, when the latter animal died, its spinal cord was made into an emulsion

TABLE 6.—*Reactions of Guinea-Pigs to the Subcutaneous Injection of Emulsions of Spinal Cords Obtained from Various Sources*

No. of Guinea-Pigs	Emulsion*	Died, Hr.			Lesion		
		12	24	48	Inflammatory	Cystic	None
4	Enteritis	0	2	0	0	4	0
4	Diphtheria	0	0	1	1	3	0
5	Scarlet fever	0	0	0	2	3	0
3	Infectious jaundice	0	1	0	1	2	0
4	Urticaria	1	3	0	0	4	0
4	Influenza	0	1	1	2	2	0
5	Pertussis	0	1	1	3	2	0
4	Poliomyelitis	0	2	2	0	4	0
1	Scarlet fever and urticaria	0	1	0	0	1	0

* An injection was given of 3 cc. of emulsion made of spinal cords of guinea-pigs that died after the injection of an emulsion made of the stools of patients with the various clinical conditions listed in the table.

TABLE 7.—*Reactions of Guinea-Pigs to the Injection of Emulsion of Spinal Cords for Many Experimental Generations*

Group	No. of Guinea-Pigs	Disease*	Experimental Generation†														
			1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
1	2	Enteritis	+	+	+	0	0	..	..	..	..	..	..	..	..	..	..
2	1	Diphtheria	0	0	..	..	..	..	..	..	..	..	..	..	..	..	..
3	1	Scarlet fever and urticaria	0	0	..	..	..	..	..	..	..	..	..	..	..	..	..
4	1	Infectious jaundice	+	0	0	..	..	..	..	..	..	..	..	..	..	..	..
5	4	Urticaria	0	0	..	..	..	..	..	..	..	..	..	..	..	..	..
6	2	Influenza	+	+	+	0	0	..	..	..	..	..	..	..	..	..	..
7	2	Pertussis	+	+	0	0	..	..	..	..	..	..	..	..	..	..	..
8	4	Poliomyelitis	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+

* These are the diseases present in the patients whose stools were used to make the emulsion that caused death in the guinea-pigs. When the stools from more than one patient were used, the report is given on that emulsion which was most virulent to the animal.

† A + sign indicates that an animal died, 0, that it lived.

which was injected into a subsequent animal. This procedure was followed for fifteen experimental generations in the case of poliomyelitis. If death did not follow the injection of the emulsions of the spinal cord, the animal was killed and the cord was removed, made into an emulsion and injected into the next series of animals. If the emulsion did not cause death in the animals it was used for only two experimental generations.

In vivo neutralizing experiments with convalescent serum were attempted. Convalescent poliomyelitis serum was added to the suspensions of the spinal cords in one set of experiments and to Rosenow's

serum in another. The combinations were incubated for one hour and then were injected subcutaneously. Practically all the guinea-pigs used as controls, as well as the animals which had been immunized, died within the first twenty-four to forty-eight hours after the injection. The time of ultimate death was actually accelerated in the protected group, although the local reaction around the site of injection in the first six hours was indurative and inflammatory and not cystic. The protected guinea-pigs were spry, ate well and were unruffled, in decided contrast to the unprotected animals. The general appearance, however, was about the same in both groups after eighteen hours had elapsed, and ultimate death occurred sooner in the protected animals than in the nonprotected group.

BACTERIOLOGY OF EMULSIONS OF THE SPINAL CORD

The spinal fluid washings of guinea-pigs that died as a result of the injection of emulsions made of stools obtained from patients with diseases other than poliomyelitis occasionally contained colon bacilli. Such findings have been attributed to agonal septicemia due to colon bacilli. The emulsions made of the spinal cords of guinea-pigs that died of injections of emulsions of stools or urine of patients with poliomyelitis always contained colon bacilli in great numbers. The emulsions of the spinal cords obtained from these animals killed other guinea-pigs, and colon bacilli were always recovered in the emulsions of the spinal cords of the latter animals. Although many emulsions made of stools of normal adults killed guinea-pigs, colon bacilli were not always found in the emulsions of the spinal cords of these animals; even when colon bacilli were found, the organism was absent in the second or third experimental generation given reinjections of emulsions of the spinal cords.

TOXICITY OF ORGANS

It would be interesting to know the comparative toxicity of organs other than the spinal cords of guinea-pigs that died after the injection of emulsions of stools of patients with poliomyelitis.

The organs of guinea-pigs and of an occasional young rabbit that died after the injection of emulsions made of stools of patients with poliomyelitis were ground in physiologic solution of sodium chloride and injected subcutaneously into test animals. These organs were standardized as follows: One Gm. each of the heart, lung, kidney, liver, adrenal gland, spleen, spinal cord, large intestine and small intestine was separately ground, and 15 cc. of physiologic solution of sodium chloride was added to each ground organ. One cubic centimeter of each emulsion contained approximately 0.06 Gm. of organ by weight. Three cubic centimeters was the dose injected.

It was found that the most toxic emulsion was always made of the small intestine. In the order named, the toxicity of the organs might be ranged as follows: small intestine, spinal cord, liver, kidney, large intestine, spleen, adrenal gland, lung and heart (table 8).

Postmortem examinations of guinea-pigs that died after the injection of emulsions of stools of patients with poliomyelitis often revealed the bladders to be dilated and filled. The walls of the bladders were seared; the urine was obtained aseptically and was found to be toxic for guinea-pigs when injected subcutaneously (table 9).

TABLE 8.—*Relative Number of Deaths in Guinea-Pigs After the Injection of Emulsions Made of Various Organs of Guinea-Pigs That Died of Injections of Emulsions of Stools of Patients with Poliomyelitis* *

No. of Guinea-Pigs	Organ Used for Emulsion†	Died	Lived
10	Small intestine	10	0
10	Spinal cord	8	2
10	Liver	5	5
10	Kidney	4	6
10	Large intestine	4	6
10	Spleen	3	7
10	Adrenal glands	2	8
10	Lung	0	10
10	Heart	0	10

* The results with rabbits' organs are not included, since only an occasional rabbit died of the injection of an emulsion of the stool of a patient with poliomyelitis.

† Each specimen was tested in only one animal.

TABLE 9.—*Toxicity of Urine Obtained Post Mortem from Guinea-Pigs That Died After the Injection of Emulsions of Stools of Patients with Poliomyelitis*

No. of Guinea-Pigs	Injection	Died, Hr.			Lesion		
		12	24	48	Inflammatory	Cystic	None
7	3 cc. of combined urine from guinea-pigs that died after injection of emulsions of stools of patients with poliomyelitis	0	7	0	0	7	0
10	3 cc. of combined urine from normal guinea-pigs that had been killed	0	0	0	7	0	3

There was no local or general reaction after the intradermal injection of emulsions made of organs of normal animals standardized as outlined in the foregoing paragraph save for a little induration in two of the thirty-six animals into which the emulsions were injected. In one of these instances an emulsion made of the small intestine and in one emulsion made of a large intestine caused the reaction.

BACTERIOLOGY OF EMULSIONS OF THE ORGANS

There was always a massive growth in the subcultures of the ground material obtained from the small intestines, large intestines, brains, livers, kidneys, adrenal glands, and spleens of animals that died after

the injection of emulsions of stools of patients with poliomyelitis. In subcultures of the heart and lungs the growths were present but were not massive.

From a morphologic standpoint only, the type of intestinal flora of these animals seemed different from that of normal animals. In smears from the intestines of normal animals the predominating organism was a gram-positive bacillus occasionally bifid or Y-shaped, with frequent sporulating forms and an occasional gram-negative bacillus. In those guinea-pigs into which were injected emulsions made of stools of patients with poliomyelitis, gram-negative organisms were the common bacteria found in both the large and the small intestine, with very few gram-positive bacteria and occasional spores. One subculture from a small intestine had a gram-positive chain coccus. Emulsions made of the intestinal contents of the guinea-pigs that died after the injection of emulsions of stools of patients with poliomyelitis were readily toxic for other guinea-pigs, as shown by the fact that subcutaneous injections of these emulsions often caused the death of the test animals in from twenty-four to forty-eight hours after the injection, while the material from the normal intestines was relatively innocuous when injected subcutaneously into other guinea-pigs.

Cultures were made on an agar medium of the contents of the small intestines of some normal guinea-pigs. The growth was scraped off, suspended in physiologic solution of sodium chloride and standardized to 0.05 cc. of organism for 3 cc. of solution of sodium chloride. This dose was injected into six guinea-pigs. Five of the six animals showed no reaction. One had some local induration. Three of the cultures had a few sparsely arranged colonies, while the other three had heavy growths. Only a few gram-negative colonies were found on smears made from the cultures.

Emulsions were also made of the contents of the large intestines of normal animals and were injected subcutaneously into six animals, with no reaction. Cultures of the contents of the large intestine showed growth in all the tubes. The organisms were chiefly gram-positive bacilli and spores. Gram-negative bacilli, although present in four of the six instances, were minor inhabitants. Subcutaneous injections of these growths into normal animals caused no reaction. Emulsions made of the contents of the gastro-intestinal tract, from either the small or the large intestines of normal animals, caused no reaction in eleven of twelve animals. One guinea-pig had a slight local induration.

Eight guinea-pigs were killed and placed in the icebox for forty-eight hours. The bodies were then sectioned, and cultures were made of the small and large intestines of each animal. Emulsions were also made of the same material and injected subcutaneously into sixteen other guinea-pigs.

One of the guinea-pigs into which was injected an emulsion made of the small intestine showed a slight thickness of the skin. The other seven did not have any reaction. None of the guinea-pigs (eight) into which were injected emulsions of the large intestines showed any reaction. There did not seem to be any increase of the colon bacteria on postmortem examination, nor, as was noted before, did death increase the virulence of the emulsion.

In seven of the cultures made of the small intestines the growth ranged from many colonies to a few, while in one the subplant had a heavy growth. In three of the cultures of the large intestines colonies were relatively sparse, while five were heavily overgrown.

On the subplant the predominant bacteria in the small intestines were gram-positive bacilli. In the cultures of the large intestines the gram-positive bacillus again predominated, a gram-negative bacillus occurring with it in the cultures from three animals. In the culture from another guinea-pig there were a few chain cocci.

In brief, specimens from organs of normal animals taken immediately after death or forty-eight hours later did not contain a factor that was toxic for other animals, and the predominant organisms in both the small and the large intestines were gram-positive bacilli.

COMMENT

Emulsions of the stools and urine from normal infants were used previously. The urine was found to be innocuous, while the stools caused death a long time after the injections were made in only three of the forty-two animals tested.

It is obvious that no claims for specificity can be drawn from these experiments. It is shown that some change occurred in the small intestines of the animals into which the injections were made, and the normal nontoxic intestinal contents were made toxic. This occurred in spite of the fact that all the injections were made subcutaneously. It suggests the possibility of local toxic accumulations in the intestines. The possibility of accumulation in excreting organs was further illustrated by the toxicity of the urine found in the bladders of the animals that died.

It is suggested, but in no wise proved, that the intestinal bacterial flora changed to gram-negative types after the injection of an emulsion made of stools of patients with poliomyelitis.

CONCLUSIONS

1. Emulsions made of the spinal cords of animals that died after the subcutaneous injection of emulsions made of stools of patients with poliomyelitis were carried in series and were found to be toxic to the fifteenth experimental generation.

2. Gram-negative bacilli were isolated from every emulsion made of the spinal cord of an animal that died after the subcutaneous injection of an emulsion made of stools of a patient with poliomyelitis.

3. The predominating organism present in the intestinal contents of normal animals was a gram-positive bacillus. In the animals into which an emulsion had been injected it was a gram-negative bacillus.

4. The organs of the animals that died after an injection ranged in toxicity as follows: small intestine, spinal cord, liver, kidney, large intestine, spleen, adrenal gland, lung and heart.

AN EVALUATION OF THE INCOMPLETE SQUARE TEST OF VISUAL ACUITY FOR YOUNG CHILDREN

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Testing visual acuity in children of preschool age has long been neglected in routine physical examinations. This failure may be due partly to the inability of children under school age and of those in kindergarten and in the first grade to read the letters of the Snellen chart and partly to a lack of confidence in the reliability of tests suited to children of these ages.

It seemed desirable, therefore, to find a test for visual acuity applicable to the child not yet able to read letters, to determine a set of standard conditions for testing which could be set up readily by the physician and to determine the reliability and validity of the test under standard conditions.

A simple test, suitable for our purposes, was described by Jackson.[1] This is the "incomplete square" test of visual acuity. The test figure is 9 mm. square; it is filled in toward the center for a distance of 3 mm. on three sides, leaving an opening on one side 3 mm. wide, as shown in the illustration. If it is placed at the center of a card 10 cm. square, it is easy to change the position of the card so as to shift the opening to any vertical or horizontal position. The child under examination is instructed to hold his or her arms in a position corresponding to the direction of the arms of the incomplete square. The child's ability to see the figure is then easily determined. Three correct readings in four trials at a distance of 10 meters is normal vision according to Jackson.[1]

TECHNIC

In this study the following conditions were selected as standard. A white blank card 28 by 46 cm. was fastened to a plain wall 140 cm. above the level of the floor. The examiner held the test card with the figure of the incomplete square on the surface of the large card. Adhesive strips were placed on the floor

From the Institute of Child Welfare, University of Minnesota.

1. Jackson, Edward: The Eyes of School Children, Am. J. Ophth. **15**:901 (Oct.) 1932.

at distances of 1 meter up to 10 meters. The shades of the room were drawn. Illumination of the test figure was kept constant by means of a 100 watt mazda electric light bulb with an aluminum student lamp reflector placed 35 cm. away from the lower edge of the card. The test was carried out by first showing the child the test figures in different positions until he was able to indicate by the position of his own arms which direction the open side of the square faced. Next, the child was placed with his toes on the 10 meter mark. The test card was shown by the examiner with both eyes of the child uncovered. Four trials were made with the incomplete square in different positions. In case of error the child was placed 1 meter closer to the figure. This distance was shortened 1 meter after each four trials until no error was made. The child was then placed again on the 10 meter line, and each eye in turn was covered with a card and the visual acuity of the other eye determined and recorded. The time required to carry out a single complete test was only a few minutes, depending, of course, on the number of errors made by the child.

EXPERIMENTAL WORK

To determine the reliability of the incomplete square test and to determine its relationship to scores on the Snellen chart, a series of tests were made on a group of kindergarten children at the Institute of Child Welfare at the University of Minnesota. Seventeen children, aged from 5 to 6 years, were tested. Ten boys and seven girls com-

The incomplete square used in the test.

prised the group. Fourteen of the group were tested on ten separate occasions at intervals of from three to ten days. Comparison of the results of the incomplete square test with those of the Snellen E test was made by testing fourteen of the children twice each with the E test at a distance of 10 meters.

In order to determine the validity of the incomplete square test as a measure of visual acuity, the total number of errors on ten trials of the incomplete square test were correlated with the total number of errors on two trials of the Snellen E test. The ranking order of correlation was found to be as follows: for vision in both eyes, 0.671, probable error 0.104; for vision in the right eye, 0.651, probable error 0.109, and for vision in the left eye, 0.559, probable error 0.130. In order to find the true relationship between the results of the incomplete square test and the results of the Snellen E test, correction was made for attenuation. The data for the right and the left eye were combined, giving twenty-eight items instead of the fourteen used in the first correlations. The true correlation between results on the two tests was found to be 0.651.

Since ten trials for each child are too many for clinical use, it was desirable to determine how many trials with the incomplete square test are necessary for a reliable test of vision. Correlations were calculated between the numbers of errors made on certain trials of the test and the total number of errors made on ten trials, the data for right and left eyes again being combined. The correlations in table 1 show the relationships. It is evident that each trial which is given increases the relationship to the total. However, three trials give sufficiently high reliability, 0.931, and three trials are practical from the standpoint of the administration of the test.

In order to determine whether or not three trials are reliable enough for testing the vision of the separate eyes, the number of errors on the first three trials was correlated with the total number of errors on ten trials, fourteen cases being used. The correlation for vision in both eyes was 0.953, probable error 0.018; for vision in the right eye,

TABLE 1.—*Correlation of Errors Made on Certain Tests with Total Errors Made on Ten Trials*

Trials	Coefficient of Correlation	Probable Error
1	0.826	0.042
1-2	0.865	0.034
1-2-3	0.931	0.017
1-2-3-4	0.940	0.016
1-2-3-4-5	0.972	0.007
1-2-3-4-5-6	0.980	0.005

0.967, probable error 0.012, and for vision in the left eye, 0.934, probable error 0.024. It is evident that the first three trials are nearly as reliable as ten trials in the determining of visual acuity by the incomplete square test.

The total number of errors made on each trial by the fourteen subjects was found, and the results were plotted by trials for vision in both eyes and for vision in the right and in the left eye. It was found that the first trial gave a high number of errors, followed in each case by a sharp drop in number of errors on the second trial, and in the case of both eyes and of the left eye there was a steady increase in errors with succeeding trials (this increase was not found with the right eye). This indicates, it seems, that the first trial is affected by lack of experience with the test and directions, that learning factors do not play a part in the results except in this initial adjustment and that perhaps the motivation is not sufficient to maintain maximum effort throughout the ten trials with children at these ages.

The fact that there is this initial falling off in the number of errors after the first trial indicates that it might be wiser to take scores for children beginning with the second trial, not counting the first trial as part of the test. There is statistical evidence supporting this in the following correlation coefficients.

Between Errors of:	Coefficient of Correlation
Trials 1, 2 and 3 and total trials	0.931
Trials 2 and 3 and total trials minus trial 1	0.920

We may conclude that the results of trials 2 and 3 are as closely related to the total as are trials, 1, 2 and 3 and are as reliable a measure of visual acuity.

TABLE 2.—*Results of Tests on Two Children Showing the Consistency of the Method*

		D. C. (Normal Acuity)										M. G. (Abnormal Acuity)									
		Meters										Meters									
	Trial	10	9	8	7	6	5	4	3	2	1	Trial	10	9	8	7	6	5	4	3	2	1
Both eyes	1	0	..	..	..	..	..	..	..	..	..	1	4	0	..	..	..	..	..	..	..	..
	2	0	..	..	..	..	..	..	..	..	..	2	0	0	..	..	..	..	..	..	..	..
	3	0	..	..	..	..	..	..	..	..	..	3	1	0	..	..	..	..	..	..	..	..
	4	0	..	..	..	..	..	..	..	..	..	4	1	0	..	..	..	..	..	..	..	..
	5	0	..	..	..	..	..	..	..	..	..	5	0	0	..	..	..	..	..	..	..	..
	6	0	..	..	..	..	..	..	..	..	..	6	0	0	..	..	..	..	..	..	..	..
	7	0	..	..	..	..	..	..	..	..	..	7	1	0	..	..	..	..	..	..	..	..
	8	0	..	..	..	..	..	..	..	..	..	8	1	0	..	..	..	..	..	..	..	..
	9	0	..	..	..	..	..	..	..	..	..	9	0	0	..	..	..	..	..	..	..	..
	10	0	..	..	..	..	..	..	..	..	..	10	0	0	..	..	..	..	..	..	..	..
		Meters										Meters									
	Trial	10	9	8	7	6	5	4	3	2	1	Trial	10	9	8	7	6	5	4	3	2	1
Right eye	1	0	..	..	..	..	..	..	..	..	..	1	4	4	1	0	..	..	..	..	..	..
	2	0	..	..	..	..	..	..	..	..	..	2	1	0	0	0	..	..	..	..	..	..
	3	0	..	..	..	..	..	..	..	..	..	3	1	0	0	0	..	..	..	..	..	..
	4	0	..	..	..	..	..	..	..	..	..	4	0	0	0	0	..	..	..	..	..	..
	5	0	..	..	..	..	..	..	..	..	..	5	1	1	0	0	..	..	..	..	..	..
	6	0	..	..	..	..	..	..	..	..	..	6	0	0	0	0	..	..	..	..	..	..
	7	0	..	..	..	..	..	..	..	..	..	7	1	0	0	0	..	..	..	..	..	..
	8	0	..	..	..	..	..	..	..	..	..	8	0	0	0	0	..	..	..	..	..	..
	9	0	..	..	..	..	..	..	..	..	..	9	0	0	0	0	..	..	..	..	..	..
	10	0	..	..	..	..	..	..	..	..	..	10	0	0	0	0	..	..	..	..	..	..
		Meters										Meters									
	Trial	10	9	8	7	6	5	4	3	2	1	Trial	10	9	8	7	6	5	4	3	2	1
Left eye	1	0	..	..	..	..	..	..	..	..	..	1	4	3	3	3	4	3	3	4	0	..
	2	0	..	..	..	..	..	..	..	..	..	2	4	2	4	2	4	2	2	0	0	..
	3	0	..	..	..	..	..	..	..	..	..	3	4	4	4	2	3	1	3	1	0	..
	4	0	..	..	..	..	..	..	..	..	..	4	2	2	4	4	3	4	3	1	0	..
	5	0	..	..	..	..	..	..	..	..	..	5	3	2	2	3	3	0	0	0	0	..
	6	0	..	..	..	..	..	..	..	..	..	6	4	4	3	3	1	4	4	1	0	..
	7	0	..	..	..	..	..	..	..	..	..	7	4	2	4	2	3	0	0	0	0	..
	8	0	..	..	..	..	..	..	..	..	..	8	4	3	4	4	4	4	4	2	0	..
	9	0	..	..	..	..	..	..	..	..	..	9	4	3	4	4	4	4	4	2	0	..
	10	0	..	..	..	..	..	..	..	..	..	10	3	4	4	4	4	4	3	0	0	..
Visual acuity		Both eyes 10/10			Right eye 10/10			Left eye 10/10				Visual acuity	Both eyes 10/10			Right eye 10/10			Left eye 10/3			

The use of trials 2 and 3 gives a slightly more valid test of visual acuity than the use of trials 1, 2 and 3, as shown by the following correlation coefficients.

Between Errors of:	Coefficient of Correlation
Trials 1, 2 and 3, incomplete square test, and total trials, Snellen E test	0.472
Trials 2 and 3, incomplete square test, and total trials, Snellen E test	0.496
Total trials, incomplete square test, and total trials, Snellen E test	0.592
Total trials minus trial 1, incomplete square test, and total trials, Snellen E test	0.632

It may be concluded, then, that the use of trials 2 and 3 as a measure of visual acuity is as reliable and slightly more valid than the use of trials 1, 2 and 3, and it is recommended that trial 1 be given but be used to accommodate the child to the examination procedure without being considered in determining the child's score on the test.

Among the children tested several had defective visual acuity. Throughout the tests the defect in visual acuity was constant. Likewise, children with normal acuity showed constant normal responses to the tests. Two examples show this (table 2).

SUMMARY AND CONCLUSIONS

1. Correlations between the results of the incomplete square test and those of the Snellen E test show that both measure the visual defects.

2. Three trials with the incomplete square test are sufficient to get reliable measure of visual acuity. The results of three trials correlate 0.931 with the results of ten trials.

3. The best measure of visual acuity is obtained from trials 2 and 3, the results of trial 1 being discarded. The second and third trials give as reliable results as the first three trials and correlate slightly higher with the results of the Snellen E test. Trial 1 is affected by unfamiliarity with the test situation and should not be included in the child's score.

4. A single child's performance is consistent through ten trials, those with visual defect showing the defect consistently and those with normal vision giving normal results throughout.

5. The incomplete square test is a reliable test of visual acuity for children of preschool age and is practical for clinical use.

RHEUMATIC PLEURISY

WITH PARTICULAR REFERENCE TO ITS DEMONSTRATION BY ROENTGEN STUDY

SAUL STARR, M.D.
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Clinically, rheumatic pleurisy is a rather uncommon syndrome. Occasionally during the course of polyarthritis the patient may complain of pain in the chest, a pleuritic friction rub is heard and the diagnosis of rheumatic pleurisy is made. Less frequently an effusion is revealed which on paracentesis proves to be an exudate. Brown [1] has emphasized the fact that pleurisy involving the interlobar pleura may not give any definite clinical signs and yet may be readily demonstrable on lateral roentgen study of the chest. With this method we have demonstrated the presence of interlobar pleurisy in a large number of our patients with active rheumatism, although the majority gave no history of a pleuritic or pneumonic episode.

REPORT OF CASES

CASE 1.—R. F., a girl aged 5 years, was admitted to the Kings County Hospital on April 30, 1934, with a complaint of sore throat, fever and pain in both sides of the chest and the right side of the abdomen. There was occasional pain in the sole of the right foot the week preceding admission. Except for infrequent sore throat there was no history of rheumatism.

The patient appeared acutely ill. She was flushed, her temperature was 104 F., the pulse rate was 120, and the respiratory rate was 40. The tonsils were small and, with the pharynx, were slightly congested. The heart was of normal size; at the apex there was a systolic blowing murmur transmitted distinctly to the left axilla. Examination of the lungs yielded negative results. There were moderate rigidity of the right upper quadrant of the abdomen and slight tenderness over McBurney's point.

In the course of the next two days a distinct pneumonic appearance developed. The abdominal pain and rigidity became so marked that acute appendicitis was seriously considered. At this time there was only questionable dulness with diminished vesicular breath sounds over the base of the right lung.

On the fourth day the joints of the fingers and toes became markedly inflamed. With salicylic therapy the acute symptoms subsided by the seventh day. On the twelfth day an elevation of temperature and a pericardial friction rub appeared, both of which persisted for a week despite treatment with amidopyrine. The

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From the Pediatric Service, Kings County Hospital, Paul Parrish, M.D., director.

1. Brown, S.: Atypical Forms of Dry Pleurisy, J. A. M. A. **102**:193 (Jan. 20) 1934.

heart rapidly increased in size to the left anterior axillary line. A double mitral murmur was heard, and the pulmonic second sound became much accentuated.

The fever and rapid pulse rate gradually subsided. Several months later, when the patient was discharged for convalescent care, the heart was slightly enlarged, and only a mitral systolic murmur was audible.

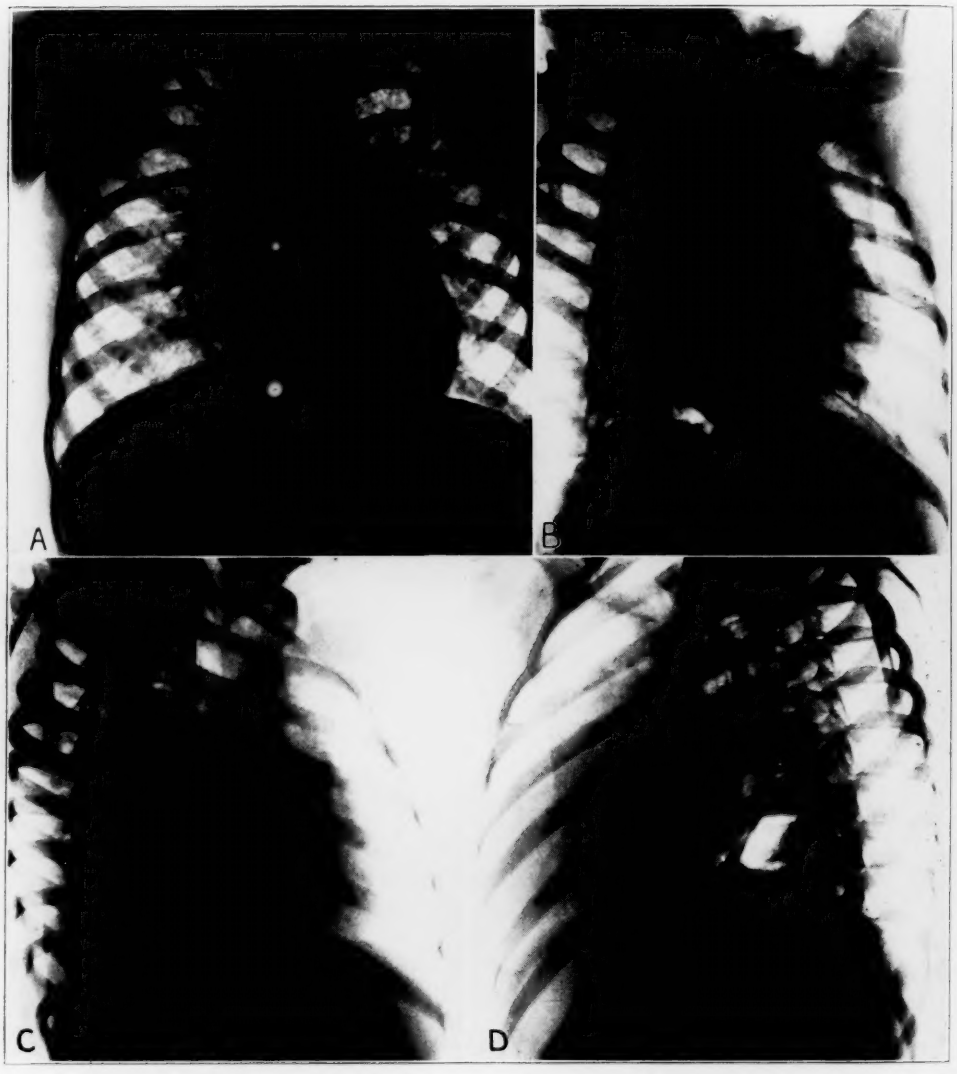

Fig. 1 (case 1).—*A* is a teleoroentgenogram showing slight infiltration at the base of the right lung. There is a prominent pulmonary conus. *B* shows a left oblique view of the chest, with thickening of the right major interlobar fissure. *C* shows the left oblique view three months later. Note the disappearance of interlobar pleurisy. *D* shows the right oblique view (esophagogram). There is marked posterior displacement of the esophagus by the enlarged left auricle.

Roentgenograms during the pleuritic attack showed a mitral heart, thickened pleura in the right minor fissure and exudate in the right major interlobar fissure extending down to the diaphragm. Roentgenograms taken later showed the pleurisy to have cleared.

The Mantoux test with 0.1 mg. of old tuberculin was negative.

The case may be summarized as follows:

Rheumatic interlobar serofibrinous pleurisy extending to become diaphragmatic, simulating acute appendicitis, was the first evidence of rheumatic fever. It was followed in four days by polyarthritis and later by pericarditis and endocarditis.

We believe the circumstantial evidence to be fairly definite that the rheumatic activity first manifested itself as interlobar pleurisy of the right lung which two days later extended down to the diaphragmatic pleura on the same side. In our other cases the evidence was less absolute.

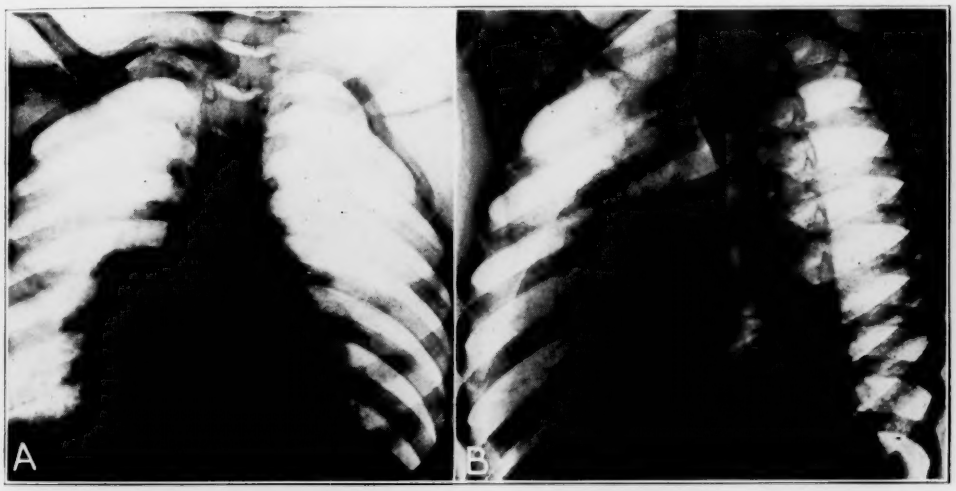

Fig. 2 (case 2).—*A*, an anteroposterior view of the chest showing bronchopneumonic infiltration at the base of the left lung. *B* shows the right oblique view (esophagogram). There is marked infiltration along the line of the left major interlobar fissure, which was not suggested in the anteroposterior view. The esophagus was displaced posteriorly.

A patient with rheumatic cardiac disease might have parietal pleurisy without simultaneous arthritis or pancarditis to serve as evidence of current rheumatic activity. Such a condition occurred in case 2.

Case 2.—V. K., a Negro girl aged 10 years, was admitted to the Kings County Hospital on Feb. 11, 1934, with a history of pain in the left side of the chest of twenty-four hours' duration, which appeared one week after a mild attack of coryza. At 9 months of age the patient had pertussis complicated by pneumonia; at 18 months she again had pneumonia. There was no history of rheumatic fever.

Pulmonary examination revealed slight dulness at the bases of the lungs, a few crepitant râles at the base of the right lung and a marked pleural friction rub at the base of the left lung. The heart was slightly enlarged, and a loud systolic apical blow was heard.

Temperature from 102 to 104 F. persisted for three days and became normal on the fifth day. On the day following admission to the hospital pain in the left side of the abdomen with rigidity appeared and lasted forty-eight hours. Moderately profuse nosebleed occurred on the same day. The right side of the chest became clear overnight, but the dulness at the base of the left lung with diminished breath sounds was present for a week.

Roentgenograms of the chest on the patient's admission to the hospital showed infiltration of the base of both lungs with pleural thickening at the base of the left lung but no fluid. Roentgenograms made at an oblique angle showed marked interlobar exudate in the left lung. The heart was slightly enlarged and of mitral configuration, the examination by way of the esophagogram showing hypertrophy of the left auricle.

The case may be summarized as follows:

Diaphragmatic pleurisy on the left side with roentgen evidence of interlobar pleurisy on the left occurred in a girl with an enlarged mitral heart and no previous rheumatic fever.

The condition in case 2 may not have been rheumatic pleurisy. Only the presence of a mitral heart and the occurrence of nosebleed caused a suspicion that the pleurisy might be rheumatic.

OBSERVATIONS

With these cases in mind and with the idea that many attacks of pleurisy in cases of rheumatic fever might be symptomless and yet might be evidenced as a thickened pleura in roentgenograms we undertook this study.

For every child with rheumatic fever admitted to the pediatric service of the King County Hospital since November 1933 teleoroentgenograms and esophagograms in both the right and the left oblique position have been made as a routine. This permits, in addition to observations on the heart, the study of the three interlobar fissures, the major fissures in the oblique views and the minor fissure in all three views.

Anatomy.—The minor fissure exists roughly as a plane running horizontally across the right side of the chest at about the level of the fourth rib. When thickened it is observed in the roentgenogram as a fine line in that position in anteroposterior, oblique or lateral views of the chest.

The major fissures, however, are planes at such an angle to the horizontal that they are visualized only in lateral or oblique views of the chest. With pleural thickening each fissure appears as a fine line extending downward and forward toward the anterior wall of the chest. In the anteroposterior view the major fissures are seldom seen.

Roentgen Findings.—Except for the distal portion of the pleura in the minor fissure, the normal interlobar pleura is not visible in roentgenograms. The minor fissure may appear in the anteroposterior view as a fine line running horizontally across the right side of the chest.

In 28 per cent of fifty-six control cases of nonrheumatic children hospitalized for various nonpulmonary conditions roentgenograms revealed this thin, short minor fissure. An abnormally thick minor fissure was present in only one case. In 7 per cent of the cases a major fissure was visualized for part or all of its course. Abnormal pleural thickening, therefore, was present in 8.9 per cent of our control series. Such thickening of fibrinous or adhesive pleurisy may be due to primary infection with pulmonary tuberculosis, nonspecific pleurisy, previous attacks of pneumonia or measles.

In a similar study of thirty-six patients with chorea admitted to the hospital during the period of study, roentgenograms of 36 per cent showed the normal thin minor fissure; those of 5.5 per cent, a much thickened minor fissure, and those of 8 per cent a thickened major fissure. Thus, 13.5 per cent showed abnormal pleural thickening.

Of eighty-five cases of rheumatism, which included all the cases of rheumatic fever exclusive of those in which the fever was associated with chorea, fibrinous or serofibrinous pleurisy was demonstrable at the bedside in six (7 per cent). By roentgenogram the following findings were noted:

	Cases	Percentage
Thickening of both major fissures	6	7.0
Thickening of right major fissure alone	21	24.7
Thickening of left major fissure alone	7	8.2
Abnormal thickening of minor fissure	20	23.5
Abnormal thickening of minor fissure alone	3	3.5
Total	57	43.6

All told, therefore, 43.6 per cent of the patients with rheumatism showed abnormal thickening of the interlobar pleura, presumably due to rheumatic pleurisy. Many of these patients showed involvement of two or three interlobar pleural surfaces at one time.

All but eight of the eighty-five patients in our series were admitted to the hospital with active rheumatic fever. If we were to eliminate these eight cases from our calculations, we should find pleurisy in thirty-six cases (46.7 per cent) of a series of seventy-seven of active rheumatic fever.

Since 12 per cent of the patients in our series with rheumatism had a positive Mantoux test and since those in our control group showed about the same percentage (8.7 per cent), we believe that there is no relationship between this high incidence of pleurisy in the children with rheumatism and that in children with primary tuberculous infection of childhood. Similarly, we find no correlation between this high incidence of pleurisy and previous illnesses, such as measles, scarlet fever or pneumonia.

We are left with the fact, that by roentgen examination 8.9 per cent of nonrheumatic children were shown to have an abnormally thickened interlobar pleura, while 46.7 per cent of children with active rheumatic fever present this finding.

In an analysis of the functional classification of the children with rheumatic cardiac disease we found the following data:

	Cases	Percentage with Pleurisy
Class 1	6 of 25	24
Class 2A	16 of 37	43
Class 2B	10 of 18	55
Class 3	5 of 15	100

At the time of discharge the patients with cardiac disease were resolved into the foregoing functional classification. With no attempt to draw any conclusions from the actual figures because of the complicating factor of more frequent pericarditis in the more severe cases, it is evident that many milder rheumatic attacks may be complicated by rheumatic pleurisy.

Children with chorea, unless there is a history of polyarthritis before the roentgenogram is taken, seem to be practically free from rheumatic pleurisy. Only one of our children with chorea showed evidence of extensive pleurisy. A roentgenogram of this boy's chest revealed thickening of the minor and major fissures on the right side. Soon after discharge he was again readmitted to the hospital with acute cardiac failure; autopsy revealed old adhesive pleurisy and pericarditis. The past history was irrelevant for all rheumatic manifestations other than chorea, and the adhesive pericarditis was not suspected.

Children with pericarditis show an extremely high incidence of pleurisy. Of fifteen children with acute pericarditis, complete roentgen studies of the chest were carried out in eleven; in eight of these thickening of the pleura was noted.

COMMENT

It is clinically impossible in most cases of rheumatism in children to obtain a history of pleuritic symptoms. We suspect that some of the febrile periods in the course of rheumatic fever may be due to deep-seated serofibrinous pleurisy which is symptomless because it never reaches the parietal pleura. Occasionally in an acute phase the pleurisy may spread along the interlobar pleura to involve the parietal or diaphragmatic pleura and cause definite symptoms, as seems to have happened in case 1.

Too little attention has been paid to an obvious discrepancy, the infrequency with which rheumatic pleurisy is seen in children in the wards and the frequency with which it is observed at autopsy. The

belief that pleurisy is a manifestation of severe rheumatic fever only would seem unjustified. Although the statement has been made that it is "generally recognized that next to cardiac involvement pleurisy is the most common complication of rheumatic fever,"[2] it is rather uncommon clinically to note rheumatic pleurisy.

Various authors quoted by Paul[2] give the incidence of pleurisy in cases of rheumatic fever as from 2 to 15 per cent, the latter figure being that of Garrod. In the most recent series published, that of Kaiser,[3] an incidence of 1.1 per cent was noted in 1,240 cases.

In his discussion of the rheumatic lung, Howard[4] he stated that "a pleurisy is found in the majority of cases that come to autopsy in either the acute or subacute stages of rheumatic fever; . . . it may exist in small patches of fibrinous exudate . . . not recognizable by any method of physical examination." He cited Thayer's series of twenty-five cases of acute rheumatic cardiac disease which came to autopsy, in 40 per cent of which serofibrinous pleurisy was noted and in one case chronic adhesive pleurisy. Our experience has shown that pleurisy in such cases is frequently symptomless and is revealed only at autopsy.

By the use of oblique roentgen views of the chest such serofibrinous pleurisy is often seen both in the early stage and in mild cases, in many instances during the first attack of rheumatic fever, as well as in severe cases of rheumatic infections.

Diaphragmatic pleurisy may be more definitely diagnosed when a roentgenogram in the oblique view shows serofibrinous pleurisy extending along an interlobar surface to the diaphragm, particularly (as in case 1) if this should subsequently disappear.

Rheumatic Pneumonia.—It is evident that since the plane of the oblique fissures is at an angle in the usual anteroposterior roentgenogram an interlobar exudate of marked degree would be interpreted as basal bronchopneumonia. If oblique views, however, show normal aeration of the lungs both behind and in front of a thickened interlobar fissure, such an error would be apparent. All cases of so-called rheumatic pneumonia should be checked by oblique or lateral views of the chest for this reason.

Rheumatic Pericarditis.—It has long been known that pleurisy occurs frequently during acute pericarditis; in fact, it has been stated that the pleurisy is an extension of the pericardial pathologic process. Some

2. Paul, J.: Pleural and Pulmonary Lesions in Rheumatic Fever, Medicine **7**:383 (Dec.) 1928.

3. Kaiser, I.: Factors that Influence Rheumatic Disease in Children, J. A. M. A. **103**:886 (Sept. 22) 1934.

4. Howard, C. P.: The Rheumatic Lung, Ann. Int. Med. **7**:2 (Aug.) 1933.

observers have found the pleurisy on the right side in more cases, others, more often on the left side. In our cases there was more often unilateral pleurisy on the right side than on the left. If it were a fact that pleurisy occurring more frequently on the left side is probably an extension from pericarditis, as has been argued, then our cases would be evidence against that view. There is no reason why rheumatic pleurisy should not be considered a primary manifestation of rheumatic fever, particularly since in so many cases with no evidence of pericarditis there is evidence of pleurisy.

The literature abounds in reports of cases in which rheumatic pericarditis was preceded by abdominal pain of such a character that the child was operated on for suspected acute appendicitis. Greengard and Hoffman [5] reported three such cases. In one of their cases the course was similar to that in our case 1, the abdominal pain being followed by polyarthritis on the fifth day and pericarditis on the seventh day. Rather than suspect pericarditis latent for seven days as the cause of the abdominal pain or any of the other considerations mentioned by the authors, such as referred pain from the pericardium, rheumatic myositis of the abdominal muscles, rheumatic peritonitis, rheumatic appendicitis or involvement of the mesenteric glands, it would seem more fitting to suspect the abdominal pain to be due, in most cases, to rheumatic diaphragmatic pleurisy.

Geissinger,[6] Hyman [7] and Tallerman [8] reported cases with an exactly similar sequence. Tallerman [8] and Giraldi [9] reported similar cases in which pericarditis did not develop.

It seems more likely, therefore, that much of the thoracic and abdominal pain in cases of rheumatic pericarditis is due to rheumatic pleurisy coming on before or during the rheumatic pericarditis.

Not in every case of rheumatic pleurisy will there be roentgen evidence of a thickened pleura. In one of the cases in which the clinical diagnosis was rheumatic pleurisy there was no roentgen evidence. The boy had a marked pleural friction rub for three days, but effusion did not develop, and there was no roentgen evidence of a thickened pleura.

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5. Greengard, J., and Hoffman, S.: Pericarditis Simulating an Acute Condition of the Abdomen, Arch. Surg. **26**:623 (April) 1933.

6. Geissinger, J. D.: Acute Abdominal Pain in Rheumatic Fever, J. A. M. A. **94**:1427 (May 3) 1930.

7. Hyman, A. S.: Abdominal Pain at Onset of Rheumatic Fever, J. A M. A. **94**:1782 (May 31) 1930.

8. Tallerman, K.: Abdominal Manifestations in Rheumatism, Brit. M. J. **2**:844 (Nov. 7) 1931.

9. Giraldi, J.: Abdominal Symptoms in Acute Rheumatism, Arch. Dis. Child. **5**:379 (Dec.) 1930.

SUMMARY

Routine anteroposterior and oblique views of the chest frequently demonstrate rheumatic interlobar pleurisy during the active phases of rheumatic fever.

By roentgen studies of an unselected series of hospitalized children, interlobar pleural thickening was demonstrated in 9 per cent of "normal" children, in 13.5 per cent of children with chorea alone and in 43.6 per cent of children with other manifestations of rheumatic fever.

The incidence of thickened pleura in the group with rheumatic infection bears no relation to the incidence of previous pneumonia, pulmonary congestion of cardiac decompensation or tuberculosis of childhood.

The greatest percentage of pleurisy was found to be associated with rheumatic pericarditis clinically, at autopsy and by roentgen examination.

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Case Reports

RARITY OF CONGENITAL MESENTERIC CYST

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The whole group of mesenteric cysts and cystic neoplasms evidently belongs to the class of pathologic rarities. Until the present time less than four hundred cases of all types have been reported in medical literature. Brunetti in 1912 collected data from all earlier literature on the subject. In his series of cases he found but twelve instances of enlargement of the abdomen at birth. Since then nine other cases of congenital mesenteric cyst have been recorded. The following case is of peculiar interest to the medical profession because it adds one more to the twenty-one rare cases already reported by medical authorities.

The first mesenteric cyst of any type was described and recorded by a Florentine physician, Benivieni, in 1507. While performing an autopsy on a boy he noted a "callus," which he considered a freak in early development. He reported it as a cyst of the mesentery. From this time until 1850 no cases were recorded except those observed post mortem. From 1880 to 1900 successful operations were reported by a few French surgeons, Péan being the first to report such an operation in 1880.

There is no general agreement of the histogenesis and the classification of cystic tumors in textbooks on surgery. The subject is by no means a settled matter among pathologists today. "It is evident that the origin of mesentery cysts has not been proved," declared Judd in 1932.

In 1900 Dowd, in a remarkable paper on mesenteric cysts, gave great impetus to the histologic, pathologic and etiologic investigation. His conclusions were accepted by such men as Moynihan, Ayers, Deaver, Niosi, Lewis, Thyng and others of his day. Dowd founded his theory on careful study of the following features: (1) life history of the patient and the cyst; (2) location of the cyst; (3) chemical composition and microscopic study of the contents of the cyst, and (4) anatomic and histologic study of the walls of the cyst. His discussion of the concurrent primitive development of the alimentary canal and the mesentery appears to strengthen his theory of embryonic origin. His paper concluded with the confident statement that if every

case were studied in accordance with the outline given the whole matter now under dispute would soon be cleared up.

These cystic tumors are among the more serious abdominal lesions; therefore, a definite understanding of their etiology, pathology and treatment has been and remains of the greatest importance. They are seldom diagnosed until operation or autopsy. This may account for the relative rarity of recorded cases. There are no pathognomonic symptoms. They may be very small or very large and may occur anywhere along the intestinal tract from the duodenum to the rectum. Approximately one half of them, however, occur in the mesentery of the small bowel, and one fourth, in the last part of the ileum. They occur singly or in multiple form, and they may be unilocular or multilocular. They are relatively rare at birth but they show an active development and are discovered more frequently after the fourth year of age. Infants in whom such cysts develop before or at birth usually die.

Since diagnosis is practically impossible except through operation or autopsy, the symptomatology is of small value. However, the symptoms usually given in reports of cases are as follows: (1) symptoms of pressure, due to enlarging cyst; (2) location of a tumor slightly to the right and below the umbilicus, freely movable in a transverse direction; (3) symptoms which simulate those of appendicitis; (4) pain, frequently present; (5) interference with functions not usually found, and (6) in the case of large accumulations, detraction from the nutrition of the body.

Differentiation from the following conditions is often exceedingly difficult: (1) acute intestinal obstruction; (2) ileus; (3) kinking; (4) volvulus, and (5) intussusception.

The Trendelenburg position may prove helpful in making a diagnosis. The prognosis is usually unfavorable, particularly in cases in which the tumor enlarges rapidly and the patient is under the fourth year of age and also in cases in which complications become a factor.

Warfield listed the following methods of treatment: (1) enucleation for the best results; (2) enucleation with intestinal resection; (3) drainage, and (4) aspiration (not recommended).

REPORT OF A CASE

History and Course.—Mrs. J. C., a secundipara, was 28 years old. Her family and personal history were negligible; the husband's health was good. She had had no miscarriages and had one healthy child, aged 7 years. Special care was given her during pregnancy. Labor occurred at term on Aug. 16, 1934. There was spontaneous delivery of a male infant, with marked dystocia during the last part of the second stage, which lasted forty minutes. The third stage was normal. The placenta showed numerous small white infarcts. The infant gave a fairly strong cry. The skin was pink except over the abdomen, where it was

markedly cyanotic. The circumference of the abdomen was 73 cm. The other measurements were normal. The baby was fairly well nourished and nursed well. Lactation began to fail in five days, and breast feeding was stopped on account of the mother's mental attitude. The infant's functions were active and normal. He would occasionally cry out from pain, and there was some vomiting. Fluid was aspirated from the abdomen above the symphysis when the child was 4½ weeks old, and 2.5 liters of viscid, clear, yellowish, mucinous fluid was removed. When the child was 9 weeks old, 1.5 liters was removed. He died in a state of marasmus at the age of 12 weeks. The cavity of the cyst had refilled to the amount of

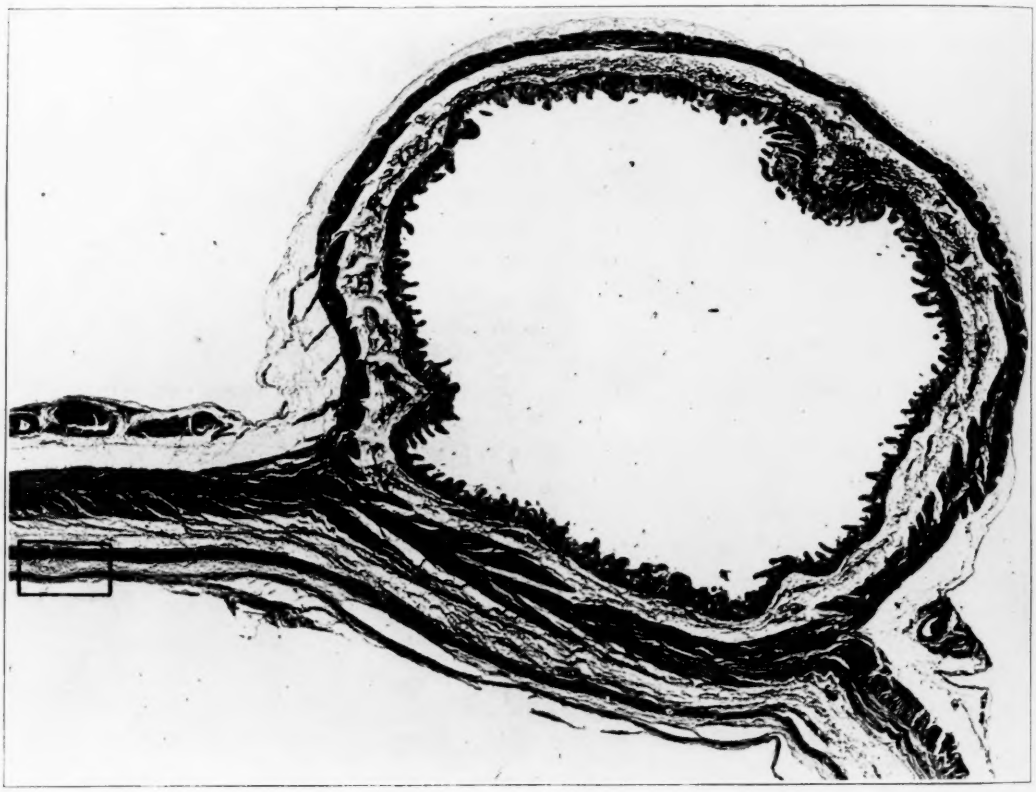

Fig. 1.—The circular structure is the intestine. The thicker structure on which it rests is a small segment of the vastly larger wall of the cyst. The intestine is normal except for slightly imperfect differentiation of the muscular layers. Where the muscle of the intestinal wall meets the cyst wall on the left of the picture, it can be distinctly seen to split, some of the outer portion being continued over the outer muscular layer of the cyst. The peritoneum of the intestine and that of the cyst are also continuous. The wall of the cyst contains all the essential structures of an intestinal wall, though the mucosa is so stretched as to be difficult to recognize. The cyst lies in the mesentery and is clearly of the alimentary (intestinal) type.

1.5 liters with fluid like that described, making a total amount of 5.5 liters. A roentgenogram taken when the child was 9 weeks old showed the liver and spleen

to be normal. Examination of the blood showed: hemoglobin, 96 per cent; red cells, 4,990,000; white cells, 12,650 per cubic millimeter; polymorphonuclears, 64 per cent. The Wassermann reaction of the infant, of the father and of the mother was negative.

Autopsy.—A report was made by Dr. W. A. Campbell: "There was practically no subcutaneous tissue. The muscles were markedly thinned in the abdominal wall. There was no free fluid in the peritoneal cavity. The large cystic tumor was elongated and roughly C-shaped. The intestines were examined. The stomach and duodenum appeared normal. The midportion of the ileum was attached to

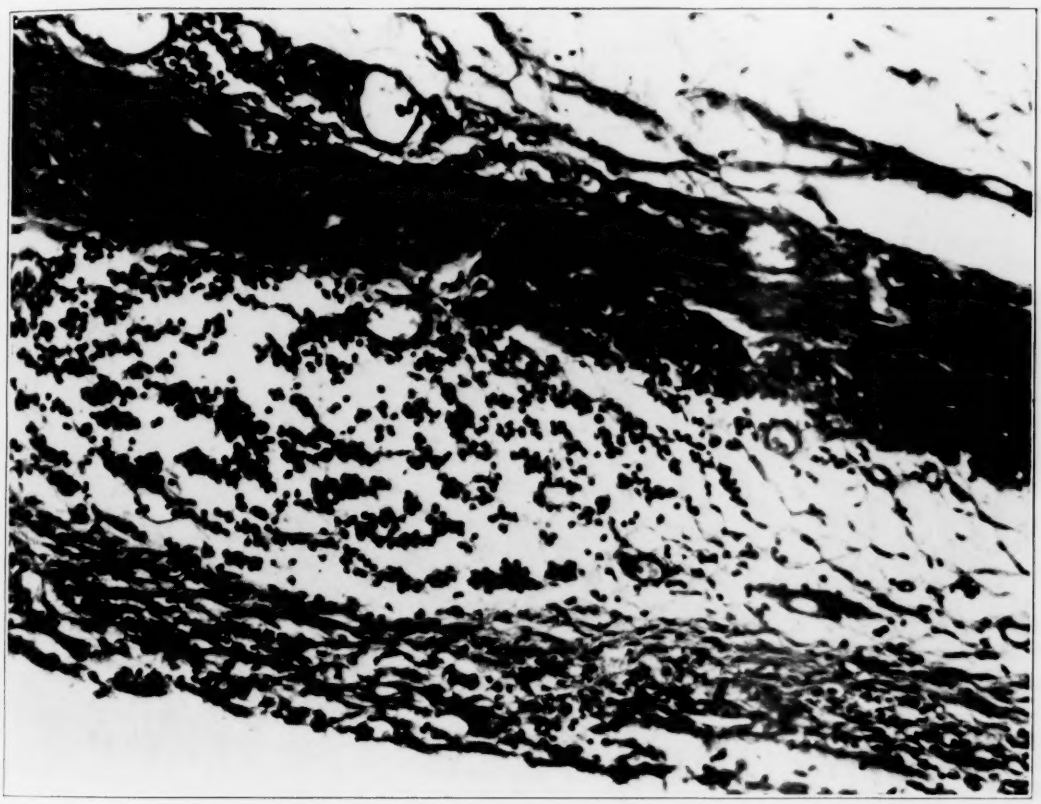

Fig. 2.—This photomicrograph shows a little of the inner portion of the wall of the cyst under high power. At the top is the stretched mucosa, containing a collection of lymphocytes. Beneath this is a layer of smooth muscle separate from the thicker layer, which was seen in figure 1 to merge with the outer muscular wall of the intestine. This separate inner layer may be regarded as a hypertrophied muscularis mucosae.

this tumor and ran along its surface for a distance of about 2 feet (60 cm.). The terminal part of the ileum was free from the tumor and entered the colon normally. The appendix and the large bowel were normal. The mass was then dissected and was found to be between the leaves of the mesentery, with a very intimate connection with the vascular supply of the bowel and the wall of the

tumor. This connection was so intimate that it was impossible to dissect the wall of the intestine from the sac. It was a thin-walled cyst. The superior mesenteric artery and vein were dissected out. The artery was found to be normal, and there was no obstruction in the vein. Apparently there was no obstruction in any of the portal circulation. The other abdominal organs were apparently normal. The spleen and liver were slightly smaller than usual but appeared normal on section. The lungs and heart were not examined. The diagnosis was congenital mesenteric cyst and marasmus."

Microscopic Examination: The cyst was multilocular and intercommunicating and ran along from the midportion of the ileum for a distance of about 90 cm. The fluid showed a specific gravity of 1.014 and contained a few blood cells but no albumin or fat globules. Microscopic examination of the wall was made by Dr. Charles T. Ryder, pathologist: "A portion of the external muscular layer split off and extended outward over the surface of the cyst, to which the intestine was closely applied. Within this there was a well developed wall of the cyst itself, composed of muscular, fatty and connective tissue, corresponding very closely to the wall of the intestine. This apparently continued over the entire specimen. The mucosa of the cyst was stretched and distorted and the epithelium, thin and broken; apart from this, the wall was typically intestinal, and the cyst was of intestinal origin rather than of lymphatic, wolffian or dermoid origin. The pathologic diagnosis was congenital mesenteric cyst of the intestinal enteric type."

COMMENT

This case is of unusual interest because of the relative rarity of the condition and because it is representative of a distinctive group of tumors which are large at birth and have a rapid course in the accumulation of fluid. It is generally conceded that a cystic tumor developing from sequestrated cells of the wolffian body is rarely found in new-born children; at least, no case has been reported thus far. Enterocystoma is more frequent; perhaps half the cases reported belong to this group. Hennig, Runkel, Hunter, Roth, Tscherning and Nasse reported cases of enterocystoma in new-born children. The patients invariably die within a few days. One will note from the history of the case reported here that the infant lived for twelve weeks.

This case may be of value in the study of mesenteric cysts because of the following factors: (1) the location of the cyst in the midportion of the ileum; (2) its close connection with and similarity in structure to the intestine; (3) its situation between the leaves of the mesentery; (4) the rapid accumulation of fluid; (5) the absence of communication between the cyst and the intestine; (6) the absence of signs of hemorrhage within the cyst; (7) the fact that the cyst was not adherent to the parietal peritoneum; (8) very definite free mobility transversely; (9) the evidences of epithelium in the wall of the cyst; (10) two layers of muscle definitely separated from each other in the wall of the cyst; (11) the splitting of the muscle layer of the intestine and its becoming continuous with that of the cyst wall; (12) the absence of intestinal obstruction but continuous narrowing of

the intestine over the cystic attachment which would soon have caused obstruction or other complications.

This cyst accumulated 5.5 liters of fluid during its life. On the presumption that the rate of accumulation did not vary, the filling of the cyst with secretion would appear to have its beginning of activity some time during the eighth month of pregnancy. The presence of epithelial cells in the wall of the cyst, when such cells are not normally found in the mesentery, suggests its origin from embryonal rests. Child's discussion of the enterocystoma and of Meckel's diverticulum, after the reports of Roth, as being of postfetal origin and not embryonic is very confusing when the salient features of this case are carefully considered.

There is a possibility that the child might have lived had the condition been recognized at the time of the first aspiration and a resection of the intestine made instead. I believe, taking all other conditions of the infant into consideration, that this was possible, even probable. Such a fortunate conclusion would, of course, have given the case far greater significance.

There is considerable question in my mind whether the classic case of Benivieni (no. *37*), which has been cited hundreds of times in reports on mesenteric cysts, is an instance of a true cyst of the mesentery. The rare old book which describes this and many other cases is written in Latin. A free translation of the description of the famous case, no. *37*, follows:

CALLUS IN VENIS MESARAICIS

Pietre Aldemari had a son who when 8 years old acquired a habit of eating earth and stones and thereby contracted a long-lasting mild fever. Afterward he began to vomit and have loose stools. Both these conditions vexed him and caused his death. When I [Benivieni] made dissection, I found a callus [hard mass] amid the veins called mesaraic. This callus obstructed the veins so that no blood could be let out of them. And this was the cause of the child's inevitable death.

Benivieni described here a solid tumor, not a cyst. The condition may have been calcification of the lymph glands of the mesentery with obliteration of the mesenteric veins. There is another case in the records of Benivieni in which the condition is closer to a true mesenteric cyst. It is described as no. *33*.

A young man named Julianus, who was always in good health, began to suffer from abdominal colic. The colicky pain augmented day by day, but nobody could discover its cause or alleviate his pain. None of the abdominal viscera gave any symptoms of sickness. Finally, the young man died. Autopsy was performed. All the internal organs were in order, but when the dissector began to dissect the intestines, his "sword" opened a large abscess which contained a large quantity of a substance dark in color and offensive in odor; this substance had the appearance of bootblack [suterium].

The odor and color of the secretion, as described, would indicate that the cyst may have had communication with the intestine. There is also the possibility of hemorrhage into the cyst.

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SUBGLOTTIC LARYNGEAL STENOSIS IN INFANCY

REPORT OF A CASE DUE TO REDUNDANCY OF THE NORMAL LARYNGEAL MUCOUS MEMBRANE

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This case is considered worthy of being reported not only because of the rarity of the underlying pathologic condition which produced the outstanding symptom, dyspnea, but because the course vividly illustrates the difficulties which may sometimes be encountered in determining the cause of this symptom in infancy.

REPORT OF CASE

The patient was a girl, born at full term and delivered by forceps. She weighed 3,680 Gm. (8 pounds and 2 ounces) at birth. The father and mother and a sister 2 years of age were in good health. The family history was otherwise irrelevant. There were no postnatal complications except that shortly after birth a red area appeared in the skin at the right corner of the mouth, which was at first thought to be an eczematous patch but was soon recognized to be a hemangioma. The patient was seen at home at the age of 1 month for the regulation of feeding. At the age of 6 weeks she was again seen at home, because of some apparent respiratory difficulty, described by the mother as perhaps a "cold." Physical examination revealed no abnormality, and with the possibility in mind that the child's respiratory difficulty might have been due to collections of mucus in the nasal passages, nose drops of ephedrine were prescribed.

When the child was 7 weeks old the father requested permission to bring her to the office one morning because during the previous night difficulty in breathing, which had been developing rather rapidly during the past three days, had become much worse. The child had had no fever but had been coughing and vomiting more or less the past few days, and her appetite was poor.

At this time the child weighed 4,700 Gm. (10 pounds and 6 ounces), and her rectal temperature was 37 C. (99.4 F.). She was well developed and well nourished. The hemangioma of the face, previously noted, had increased somewhat in size. The child was breathing with great difficulty, with a marked inspiratory stridor and with infrasternal and suprasternal retraction. There was no cyanosis,

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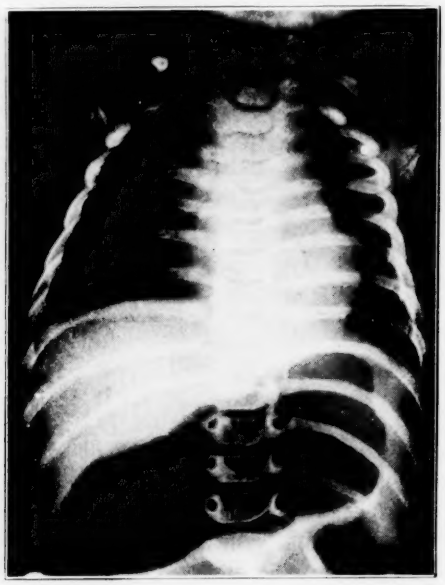
and the voice when the infant cried seemed normal. Digital examination of the larynx revealed no abnormality. There was marked dulness to percussion beneath and lateral to the first portion of the sternum. No abnormal mass could be felt in the suprasternal notch. The impression was that the child had an intrathoracic mass, probably a large thymus gland, which was causing symptoms by pressure on the trachea or bronchi. This was confirmed by a fluoroscopic examination and a roentgenogram of the chest (fig.). The trachea appeared deviated to the right and partially compressed. A lateral roentgenogram of the thorax was not completely satisfactory but showed a thoracic mass having the position of an enlarged thymus gland.

While the films were being developed, the dyspnea increased, there were retractions of the ribs laterally and the child became slightly cyanotic. The infant was rushed to a hospital, where the roentgenologist confirmed the diagnosis of an



Anteroposterior roentgenogram showing widening of the thymic shadow and deviation and compression of the trachea.

enlarged thymus gland after examination of the wet films and the patient was given a roentgen treatment. Following the treatment special nurses were employed to give the child oxygen by means of a nasal funnel, and it was confidently expected that within twenty-four hours the child would show marked improvement. The following morning, however, she seemed no better. There were rare moments when she seemed to breathe with ease, but most of the time dyspnea was intense, with marked retraction of the soft parts of the thorax, opisthotonos and slight cyanosis. It was evident that the child could not go on in that manner very long. An otolaryngologist was consulted regarding the advisability of direct laryngoscopy, bronchoscopy or tracheotomy. He decided that the infant's condition was too critical to permit any diagnostic or operative procedure and that death would probably occur in a few moments. His impression was that the child had some kind of intrathoracic tumor, possibly an abnormal thymus gland. Another otolaryngologist gave the same opinion.

For the purpose of securing a more adequate supply of oxygen, the infant was transferred to the Strong Memorial Hospital, where an oxygen tent was available. A 10 per cent solution of dextrose was administered intramuscularly [1] with the idea of supplying dextrose and also with the thought that because of the extreme hydrolability of the thymus gland the hypertonic solution might relieve some of the congestion in the organ producing the obstruction. The child seemed to do very well in the oxygen tent, at times having periods of normal breathing. The following morning the child was seen in consultation with Dr. S. W. Clausen, who noted an impaired percussion note beneath the sternum and suspected that the failure of response to roentgen therapy might be due to the presence of some tumor not thymic. A third nose and throat consultant decided against laryngoscopy or bronchoscopy. A roentgenogram of the chest was made, which showed considerable apparent diminution in the size of the thymus, but despite this another roentgen treatment was administered. The following day the child seemed much better and was taken out of the oxygen tent; the next day she was discharged from the hospital.

Two weeks later, at the age of 2½ months, the child was again admitted to the hospital because of dyspnea. In the interval she had had one roentgen treatment of the thymus gland, and until four days previous to the admission she had done very well. It was now thought that the child had an intrathoracic tumor, which was not apparently simple hypertrophy of the thymus. A clue to the possible nature of the tumor was given by the observation that the hemangioma on the child's face had increased progressively in size. Because of this it was thought that the tumor might be an angioma of the thorax, though this is one of the rarest of intrathoracic tumors.[2] If this were true, it would also explain in part the occasional remissions of the dyspnea.

Dr. John J. Morton, who had observed the patient since her original admission to the hospital, felt, as did her other physicians, that the child probably had an intrathoracic neoplasm. As it seemed evident that the infant would die if not relieved, it was decided to explore the thorax. This was done with the patient under ether anesthesia, the sternum being split from the jugular notch to the xiphoid process. Ether-oxygen anesthesia with positive pressure was then administered; the pleura was reflected laterally on each side without opening, and a mass having the appearance of a normal thymus gland presented itself. This was completely dissected out and weighed 12 Gm., which is toward the smaller limit of normal weight (from 10 to 20 Gm.) given by Boyd [3] for the thymus gland in infants of this age. It is interesting that despite the intensive roentgen treatment to which the gland had been subjected it appeared microscopically like normal thymus tissue. This seems unusual, because the normal reaction of the thymus gland to roentgen therapy is fibrosis.[4] Visual and digital examination of the thoracic cavity gave no evidence of any unusual mass.

The duration of the operation from the time anesthesia was induced until it was discontinued was not over forty-five minutes. The infant stood the operation,

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2. Michaelis, O.: Die intrathorakalen cystischen Lymphangiome, Deutsche Ztschr. f. Chir. **242**:250 (Jan. 8) 1934.

3. Boyd, E.: Variability in Weight of the Thymus and Its Component Parts in Health and Disease, Am. J. Dis. Child. **46**:1163 (Nov.) 1933.

4. Friedlander, A.: Diagnosis and Treatment of Enlarged Thymus, Am. J. Dis. Child. **6**:38 (July) 1913.

which has an average mortality of about 33.3 per cent,[5] very well, and when returned to the oxygen tent she was breathing normally. It was felt that the cause of the difficulty had been finally removed. The infant was discharged thirteen days after operation, at the age of 3 months. A roentgenogram of the chest was made the previous day. At the time of discharge the infant had moderate dyspnea with beginning bulging of the sternum and depression of the ribs on each side, resembling a marked Harrison groove. The respiratory difficulty was attributed by the surgeons to loss of a fixed thoracic point, and it was believed that as soon as bony union was firmly established the dyspnea would disappear.

Four days after her discharge it was necessary to readmit the patient because of difficulty in breathing, which had progressively increased, and vomiting. Through the efforts of respiration the thoracic cage was markedly deformed. Because of the vomiting, the possibility that the respiratory obstruction might be due to some tumor which was encroaching both on the lumen of the esophagus and on the trachea or bronchi was considered. A mixture of barium sulphate was administered, but the results of the examination showed the esophagus and the stomach to be normal. The thought then occurred that if the bronchial tree could be visualized by some opaque medium, such as iodized poppy-seed oil, any deformity sufficient to produce such marked obstruction might be localized. We could find no record at that time, nor have we found one since then, of the use of iodized poppy-seed oil for such a young infant, but as the situation was desparate, 5 cc. of warm iodized poppy-seed oil, 40 per cent, was injected (by Dr. Heatly) into the trachea with direct laryngoscopic observation. At that time it was noted that the subglottic tissues appeared markedly swollen, but the child's condition was too critical to permit a more thorough study. Roentgenograms made a few minutes afterward gave excellent visualization of the bronchial tree.

After examination of these films it was decided that the respiratory obstruction was not in the thoracic portion of the trachea but was limited to the subglottic region. Tracheotomy was therefore performed, with immediate relief of the dyspnea. A few days later a careful direct laryngoscopic examination was made. The epiglottis, the ventricular bands and the true vocal cords appeared normal. The subglottic space presented a most interesting picture. A thick band of somewhat reddened tissue projected beneath each vocal cord, reducing the lumen to a narrow chink. Probing demonstrated this tissue to be soft and readily displaced. It presented none of the characteristics of a hemangioma. In the opinion of the laryngologist it represented an unusual redundancy of the subglottic tissue. The diameter of the subglottic space in infants of this age is normally not over 6 to 7 mm.,[6] and the mucous membrane is quite vascular. Because of this normally narrow space, any redundancy of the mucous membrane will dangerously diminish the air passage.

After the infant had recovered from the effects of the tracheotomy, she was subjected to periodic dilatation of the subglottic obstruction, starting with a no. 14 metal bougie and gradually increasing to a no. 24. Nine treatments were given over a period of sixteen weeks, progressive improvement being noted each time. The child was prepared for the procedures by small doses of phenobarbital and atropine, and the treatments appeared to cause little subsequent discomfort. After five weeks of treatment the infant could breathe fairly well on occlusion of the tracheotomy tube; after thirteen weeks the tracheotomy tube was removed. When

5. Parker, C. A.: Surgery of the Thymus Gland: Thymectomy; Report of Fifty Operated Cases, Am. J. Dis. Child. **5**:89 (Feb.) 1913.

6. Tucker, G.: The Infant Larynx: Direct Laryngoscopic Observations, J. A. M. A. **99**:1899 (Dec. 3) 1932.

the patient was last examined, at the age of 9 months, breathing was normal and the subglottic bands appeared to have retracted to the edges of the vocal cords. The infant's progress was otherwise uneventful, except that the hemangioma of the face offered considerable difficulty to the dermatologist who had charge of its treatment. The thoracic deformity gradually disappeared, and even the scars of the tracheotomy and thoracotomy, which healed well without keloid formation, were not especially noticeable.

COMMENT

Congenital hyperplastic redundancy of the normal subglottic mucous membrane of the infantile larynx sufficient to cause obstructive dyspnea has not been previously described so far as we have been able to discover. The presence of a large thymus gland in our patient drew attention from the larynx to the thorax. That this is not an uncommon error is indicated by the experience of Kennedy and New.[7] They reviewed thirty cases of congenital stridor in patients admitted to the Mayo Clinic over a period of ten years. Fifteen patients (50 per cent) were admitted with stridor as the chief complaint, and in the cases of nine of these a diagnosis of enlarged thymus had been made. In all but one case roentgen therapy had been administered without any benefit. In thirteen cases it was possible to make a final diagnosis, and in only one case was this diagnosis tumor of the thymus gland. The other cases comprised eight of congenital relaxation of the larynx and one each of tracheal subglottic diaphragm, laryngospasm, multiple papilloma of the larynx and stridor due to cerebral palsy. It seems desirable that in the presence of obstructive dyspnea the pediatrician should insist on direct examination of the larynx, even when broadening of the superior mediastinal shadow in the roentgenogram indicates that compression of the thoracic portion of the trachea is the probable cause. This does not mean that congenital stridor does not occur owing to enlargement of the thymus, and the possibility of stridor from this cause must always be kept in mind.[8] If the thymus gland is merely suspected as the cause of stridor and there is no relief within twenty-four hours after roentgen therapy, an absolute indication for direct inspection of the air passages exists. The successful use of iodized poppy-seed oil in our case suggests that it may perhaps be more freely used than it has been hitherto in the diagnosis of intrathoracic conditions in early infancy. Because of our experience with this patient, we were able to demonstrate by means of iodized poppy-seed oil an intrathoracic mass causing tracheal deformity in another infant of about the same age.

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7. Kennedy, E. L. J., and New, G. B.: Chronic Stridor in Childhood, Sometimes Erroneously Attributed to Enlargement of the Thymus, J. A. M. A. **96**:1286 (April 18) 1931.

8. Friedlander.[4] Parker.[5] Tucker.[6] Kennedy and New.[7] Crotti, A.: Thymic Tracheostenosis and Thymic Death with Report of Cases, J. A. M. A. **60**:571 (Feb. 22) 1913.

SICKLEMIA IN THE MEXICAN RACE

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Sickle cell anemia and the sickling phenomenon are generally considered to be found only in Negroes or in persons having an admixture of Negro blood. A review of the literature, however, shows reports of several cases in which the possibility of Negro blood in the patient is remote.

Archibald [1] reported a case of sickle cell anemia in an Arab, and Stewart [2] reported one in a Cuban; in neither could the possibility of Negro blood be excluded. On the other hand, Castana [3] reported a case of sickle cells in an Italian child, and Cooley and Lee [4] reported a typical case in a Greek child, in whom the possibility of Negro blood was improbable. Rosenfeld and Pincus [5] described an instance of a child of Mediterranean parentage with sickle cell anemia, in whom the presence of Negro blood was not possible, as the family had lived in the same town for generations and Negroes were unknown in that community. More recently, Sights and Simons [6] added a well marked case in a man of Scotch-Irish ancestry, and Clarke [7] reported this dyscrasia in two white children of Italian parentage.

Read before the Dallas Society of Experimental Medicine (in abstract) on May 10, 1934.

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4. Cooley, T. B., and Lee, D.: Sickle Cell Anemia in a Greek Family, Am. J. Dis. Child. **38**:103 (July) 1929.

5. Rosenfeld, S., and Pincus, J. B.: Occurrence of Sicklemia in the White Race, Am. J. M. Sc. **184**:674 (Nov.) 1932.

6. Sights, W. P., and Simons, S. D.: Marked Erythrocytic Sickling in a White Adult Associated with Anemia, Syphilis and Malaria, J. Med. **12**:177 (June) 1931.

7. Clarke, F.: Sickle Cell Anemia in the White Race, with Report of Two Cases, Nebraska M. J. **18**:376 (Oct.) 1933.

Thus the finding of the sickling phenomenon in Mexican women of the same family in whom no history of Negro blood could be elicited seems to merit being reported in this paper.

Herrick [8] described sickle cell anemia completely in 1910, and since that time Sydenstriker,[9] Huck,[10] Rich,[11] Hahn and Gillespie,[12] Jaffé,[13] Anderson and Ware [14] and Diggs,[15] as well as some of the English writers, have described fully the anemic and nonanemic phases of this clinical condition as seen in the Negro race.[16]

As to the etiology of sickle cell anemia and sicklemia, it is a familial disease and appears to be transmitted, according to the mendelian law, as a dominant factor. It seems to occur most frequently in Negro men, chiefly in young men. Jaffé, Anderson and Ware, Syndenstriker and Diggs carefully analyzed and described the pathogenesis of this condition.

The mechanism of the formation of the sickled red cells has been explained by several theories, each having a certain amount of experi-

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9. Sydenstriker, V. P.: Sickle Cell Anemia and Sicklemia, in Christian, H. A., and Mackenzie, James: Oxford Medicine, New York, Oxford University Press, 1920, vol. 2, pt. 2, p. 649. Sydenstriker, V. P.; Mulheim, W. A., and Houseal, R. W.: Sickle Cell Anemia: Report of Two Cases in Children with Necropsy in One Case, Am. J. Dis. Child. **26**:132 (Aug.) 1923. Sydenstriker, V. P.: Sickle Cell Anemia, South. M. J. **17**:177 (March) 1924; Sickle Cell Anemia, J. A. M. A. **83**:12 (July 5) 1924; Sickle Cell Anemia, M. Clin. North America **12**:1451 (March) 1929.

10. Huck, J. L.: Sickle Cell Anemia, Bull. Johns Hopkins Hosp. **34**:335 (Oct.) 1923.

11. Rich, A. R.: The Splenic Lesion of Sickle Cell Anemia, Bull. Johns Hopkins Hosp. **43**:397 (Dec.) 1928.

12. Hahn, E. V., and Gillespie, E. B.: Sickle Cell Anemia: Case Greatly Improved by Splenectomy; Experimental Study of Sickle Cell Formation, Arch. Int. Med. **39**:233 (Feb.) 1927.

13. Jaffé, R. H.: Die Sichelzellenanämie, Virchows Arch. f. path. Anat. **265**: 452, 1927.

14. Anderson, W. W., and Ware, R. L.: Sickle Cell Anemia, Am. J. Dis. Child. **44**:1055 (Nov.) 1932; Sickle Cell Anemia, J. A. M. A. **99**:902 (Sept. 10) 1932.

15. Diggs, L. W.: Blood Picture of Sickle Cell Anemia, South. M. J. **25**:615 (June) 1932. Diggs, L. W., and Cheng, R. W.: Sickle Cell Anemia: A Case with Necropsy in an Adult on Whom Splenectomy Was Attempted, Arch. Int. Med. **51**:100 (Jan.) 1933. Personal communications with L. W. Diggs.

16. Since the completion of this paper, two cases of sickle cell anemia have been reported in a typical Midwestern American family without suspicion of Negro or Southern European ancestry (Cooke, J. V., and Mack, J. Keller: Sickle-Cell Anemia in White American Family, J. Pediat. **5**:601 [Nov.] 1934).

mental support. The studies of Hahn and Gillespie and Scriver and Waugh [17] are the most complete and convincing.

The pathology has been adequately described by Sydenstriker, Rich, Steinberg and Diggs.

The blood picture and the technic of its determination have been carefully studied and described by Sydenstriker, Diggs and others.

The symptomatology and the physical findings have been discussed, evaluated and reported in detail by Anderson and Ware, by Diggs and by Leivy and Schnabel.[18]

The results of roentgen examinations have been described and reported by Moore,[19] LeWald [20] and Brandau.[21]

The treatment of sickle cell anemia and sicklemia is still in the experimental stage, and though there is still much disagreement among authors concerning this aspect of the disease, the conclusions drawn by Diggs seem to be the best to date.

During the routine examination of Mexican school children in the Mexican Methodist Mission, our curiosity was aroused by a patient (case 1) because of her marked pallor and the peculiar greenish tint which was present in the conjunctivae and the buccal mucous membrane. Examinations of the blood revealed a rather marked secondary anemia, and the direct smears stained with Wright's stain showed much anisocytosis and poikilocytosis and many oat-shaped red cells. Wet smear preparations were made which showed 70 per cent sickling in twenty-four hours. Subsequent examinations were made on this patient and on 2 sisters, 3 brothers, mother, father, maternal grandmother and maternal grandfather. Sickling was found in her sister (case 2) and in her mother (case 3). Her brothers, grandparents and father were normal (fig. 1 and table 1). Owing to the presence of sickling in this family, 139 additional Mexican children between the ages of a few months and 15 years were examined for the sickling phenomenon. A series of 100 apparently normal adults between the ages of 18 and 70 were examined. No sickling was demonstrable in the latter groups (table 2).

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17. Scriver, J. B., and Waugh, T. R.: Studies on a Case of Sickle Cell Anaemia, Canad. M. A. J. **23**:375 (Sept.) 1930.

18. Leivy, F. E., and Schnabel, T. L.: Abdominal Crises in Sickle-Cell Anemia, Am. J. M. Sc. **183**:381 (March) 1932.

19. Moore, S.: X-Ray Findings in Sickle Cell Anemia, J. Missouri M. A. **26**:561, 1929.

20. LeWald, L. T.: X-Ray Findings in Sickle Cell Anemia, in Waters, C. A., and Kaplan, Ira J.: Year Book of Radiology, Chicago, Year Book Publishers, Inc., 1932, p. 76; ibid., 1933, p. 337.

21. Brandau, G. M.: Incidence of Sickle Cell Trait in Industrial Workers, Am. J. M. Sc. **180**:813 (Dec.) 1930. Steinberg, B.: Sickle Cell Anemia, Arch. Path. **9**:876 (April) 1930.

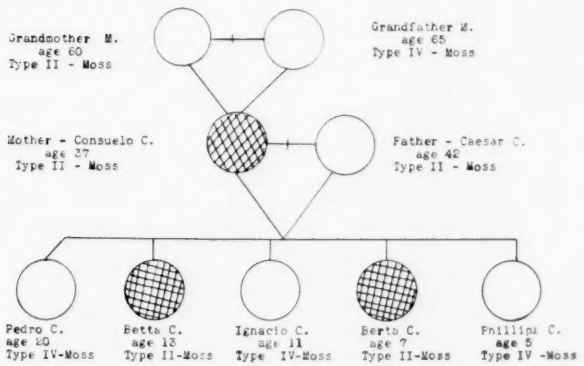

Fig. 1.—The diagram shows sickling in three generations of a Mexican family (C.). The checked circles indicate the presence of sickling, and the blank circles, its absence.

TABLE 1.—*Blood Studies of Mexican Patients with Sickling*

	On Admission	2 Weeks Later	4 Weeks Later	6 Weeks Later	12 Weeks Later
Case 1*					
Hemoglobin (Sahli), per cent	62	73	75	74	75
Erythrocytes	3,210,000	3,500,000	3,590,000	3,480,000	3,510,000
Leukocytes	9,950	8,000	8,600	10,000	9,300
Polymorphonuclears, per cent	75	77	65	78	60
Lymphocytes, per cent	16	13	25	21	25
Monocytes, per cent	7	6	7	1	10
Eosinophils, per cent	2	4	3	0	5
Band forms, per cent	14	10	11	9	7
Mature forms, per cent	61	67	54	69	53
Sickling, per cent in 24 hours	70	70	70	70	70
Case 2†					
Hemoglobin (Sahli), per cent	68	70	70	65	68
Erythrocytes	3,380,000	3,700,000	3,750,000	3,400,000	3,500,000
Leukocytes	10,600	9,800	9,100	9,700	9,900
Polymorphonuclears, per cent	77	75	76	79	74
Lymphocytes, per cent	14	20	20	11	24
Monocytes, per cent	3	1	2	6	0
Eosinophils, per cent	6	4	2	4	2
Band forms, per cent	15	12	11	9	10
Mature forms, per cent	62	63	65	70	64
Sickling, per cent in 24 hours	60	50	50	50	50
Case 3‡					
Hemoglobin (Sahli), per cent	80	81	82	80	80
Erythrocytes	4,100,000	4,250,000	4,300,000	4,000,000	4,150,000
Leukocytes	7,200	7,500	7,700	7,000	7,300
Polymorphonuclears, per cent	65	70	68	66	70
Lymphocytes, per cent	20	21	22	23	25
Monocytes, per cent	10	5	8	7	2
Eosinophils, per cent	5	4	2	4	3
Band forms, per cent	10	6	8	7	10
Mature forms, per cent	55	64	60	59	60
Sickling, per cent in 24 hours	80	80	80	80	80

* Normal sedimentation rates; no tubercle bacilli in the sputum; reticulocytes, 1.6 per cent; blood group, II (Moss); Kahn reaction, negative; direct blood smear, marked poikilocytosis, some anisocytosis and many oat-shaped red cells.

† Normal sedimentation rate; no tubercle bacilli in sputum; reticulocytes, 1 per cent; blood group, II (Moss); Kahn reaction, negative; direct smear, slight poikilocytosis.

‡ Normal sedimentation rate; reticulocytes, 0.5 per cent; blood group II (Moss); Kahn reaction, negative.

REPORT OF CASES

CASE 1.—In October 1933 B. C., a Mexican girl aged 13, came to the Mexican Methodist Mission because of a persistent cough, weakness, pallor and failure to gain weight. The cough was of three weeks' duration and nonproductive, but it was harsh and at times caused knifelike pain. She stated that at irregular periods she had a slight rise in temperature in the afternoon. Subsequent quizzing revealed that she was afraid she might have tuberculosis because she had been in contact with several persons known to have it. There was no history of tuberculosis in the family. Physical examination revealed a poorly nourished and poorly developed girl with slight pallor. The head and scalp showed no irregularities or abnormalities. The nose and ears showed no obstruction or discharge. The eyes reacted to light and in accommodation, but the scleras were pale, with a peculiar greenish tint. The teeth were carious, and the gums showed mild gingivitis. The tonsils were large, beefy and cryptic. The pharynx was moderately inflamed and injected. The mucous membranes of the oral cavity were distinctly greenish. The tongue was coated. The cervical glands were slightly enlarged but not tender. The chest

TABLE 2.—*Number of Persons Whose Blood Was Examined for Sickling*

	Total	Male	Female
Mexican children*	139	61	78
Normal healthy Mexican children	67	31	36
Abnormal Mexican children	72	30	42
Clinical diagnoses:			
Tuberculosis	15	2	13
Syphilis	6	3	3
Upper respiratory tract diseases	79	34	45
Genito-urinary diseases	10	3	7
Miscellaneous diagnoses	29	19	10
Mexican adults†	100	40	60

* The average age of Mexican children was 11.3 years. The youngest child was 3 weeks old; the oldest, 15 years.

† The average age of the Mexican adults was 39.5 years. The youngest person was 18 years old; the oldest, 73 years.

showed normal symmetry and expansion. There were no areas of consolidation and no râles. The breath sounds were slightly more pronounced than is usual, especially over the larger bronchi. The heart was not enlarged. There were no murmurs or thrills. The apex beat was in the fifth costal interspace in the middle clavicular line. Blood pressure was 100 systolic and 72 disastolic. The abdomen was flat, and there were no areas of tenderness or rigidity. The viscera could not be felt. The external genitalia were normal. A vaginal examination was not made.

The extremities showed no irregularities or abnormalities. Reflexes were all present and normal.

The laboratory examination showed: hemoglobin, 52 per cent (Sahli); red blood cells, 3,210,000; white blood cells, 9,950; polymorphonuclears, 75 per cent; lymphocytes, 16 per cent; monocytes, 7 per cent; eosinophils, 2 per cent; Schilling band forms, 14 per cent, and mature forms, 61 per cent. Direct smears showed marked poikilocytosis, some anisocytosis and many oat-shaped red cells. The sedimentation rate was normal. The sputum did not show tubercle bacilli on repeated examination. The reticulocytes averaged 1.6 per cent. The blood was of group II (Moss). A roentgenogram of the chest revealed no pathologic condition. The Kahn test gave negative results. Wet blood smear preparations showed 70 per cent sickling in twenty-four hours.

The patient was placed on a diet high in calories and vitamins with cod liver oil. After ten days the cough had disappeared, and the patient was improved both subjectively and objectively. Hemoglobin estimations at the end of two weeks, four weeks, six weeks and twelve weeks after admission were 68 per cent, 73 per cent, 75 per cent and 75 per cent (Sahli), respectively. At these intervals the wet smear preparations continued to show sickling, with the original percentage.

CASE 2.—B. C., aged 7, sister of B. C. (case 1), was seen in the mission at the same time as her sister. Her chief complaints were frequent colds and sore throat with some slight elevation of temperature and general malaise. The colds and sore throats occurred from eight to ten times per year and hung on for several weeks. The rest of the patient's history was irrelevant except for frequent contact with persons known to have tuberculosis. Physical examination showed large

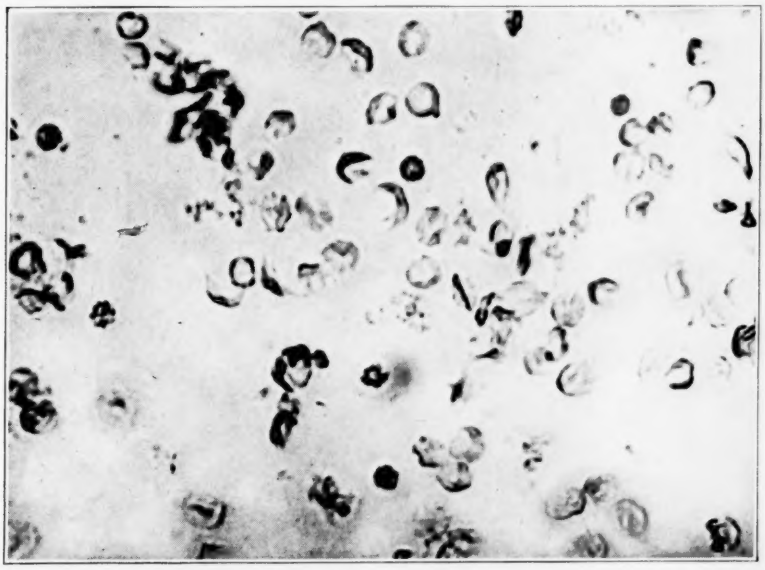

Fig. 2.—Photomicrograph showing sickling after twenty-four hours (case 1) (wet blood smear preparation; oil immersion).

beefy tonsils, a reddened and inflamed pharynx, a nasal and postnasal discharge of a seropurulent nature and moderate nontender cervical adenopathy. The examination otherwise gave normal results except for a systolic murmur at the apex, which was not transmitted and was considered to be functional in nature by the cardiac consultant.

The laboratory examination showed: hemoglobin, 68 per cent (Sahli); red blood cells, 3,380,000; white blood cells, 10,600; polymorphonuclears, 77 per cent; lymphocytes, 14 per cent; monocytes, 3 per cent; eosinophils, 6 per cent; Schilling band forms, 15 per cent, and mature forms, 62 per cent. The sedimentation rate was normal. The sputum did not show tubercle bacilli on repeated examinations. The reticulocytes averaged 1 per cent. The blood was of group II (Moss). Direct smears showed slight anisocytosis and poikilocytosis. The Kahn test gave negative results. Wet blood smear preparations showed 60 per cent sickling in twenty-four hours.

The patient was given symptomatic treatment and advised to have a tonsillectomy, but consent was refused. Estimations of hemoglobin at the end of two weeks, four weeks, six weeks and twelve weeks showed 70, 70, 65 and 68 per cent, respectively. The general condition was only slightly improved. The percentage of sickling remained the same in the wet smear preparations made along with the estimations of hemoglobin.

CASE 3.—C. C., the mother of the two patients already described, was seen in the mission with her daughters. She had no complaints and came for no treatment. History and physical examination were uninformative, but owing to the presence of sickling in her children, wet smear preparations of her were made. This procedure was carried out on all members of this family (fig. 1).

The laboratory examination on admission showed: hemoglobin, 80 per cent; red blood cells, 4,100,000; white blood cells, 7,200; polymorphonuclears, 65 per cent; lymphocytes, 20 per cent; monocytes, 10 per cent; eosinophils, 5 per cent; Schilling band forms, 10 per cent, and mature forms, 55 per cent. The blood was of group II (Moss). The Kahn test gave negative results. Wet smear preparations showed 80 per cent sickling in twenty-four hours. The percentages for hemoglobin and sickling remained unchanged during four subsequent examinations at two week, four week, six week and twelve week intervals.

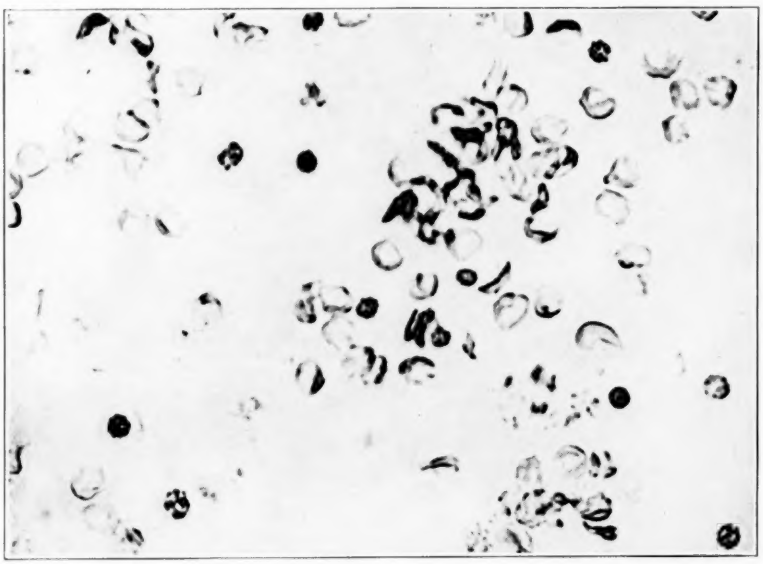

Fig. 3.—Photomicrograph showing sickling after eighteen hours (case 2) (wet blood smear preparation; oil immersion).

COMMENT

In view of the finding of sickling in this isolated Mexican family, their family history was investigated as far as possible. The mother and father were peons, born and reared in the interior of Mexico near Mexico City. The oldest daughter had been born in Mexico, but the

other children were American-born. The paternal grandparents were dead of causes unknown. The maternal mother and the maternal father were living and well. The mother stated that her forebears were Aztec Indian in origin. The father was unable to say whether his family was of Indian origin or not. Both the mother and the father denied the presence of Negro blood in their families. None of the members of the family had the facies or characteristics of the Negro.

It is of importance here to state that Moore, in his report on the roentgen findings in persons with sickle cell anemia, referred to some work of Williams, who had observed osseous changes in Mayan skulls from Yucatan which are identical with those considered by LeWald and himself as pathognomonic of sickle cell anemia. He further advanced the conjecture that perhaps the wide prevalence of sickle cell anemia or of some similar dyscrasia of the blood played a part in the downfall of the Mayan civilization. These interesting items may explain the presence of sicklemia in the Mexican people, as they are genetically closely related to the primitive people of Central and South America.

CONCLUSIONS

1. The sickling phenomenon (sicklemia) is reported for the first time in Mexicans.

2. A review of the literature is made.

3. No history or evidence could be elicited to show there was an admixture of Negro blood present in this family.

4. An explanation of the phenomenon in Mexicans is offered.

Progress in Pediatrics

DIABETES MELLITUS WITH EXTENSIVE GANGRENE IN EARLY INFANCY

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AND
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Although reports of diabetes with the onset in early infancy are being added to the literature with increasing frequency, the condition in this age group is still sufficiently rare to be of unusual interest. We propose first to report a case that we have observed in which there appears to have been more extensive gangrene than in any similar case heretofore reported; secondly, to review the previously reported cases of gangrene associated with diabetes in infancy, and finally, to tabulate and discuss our collection from the literature of case reports of diabetes with onset in children under 1 year of age.

REPORT OF A CASE

Our patient was a Negro boy aged 3 weeks, who was admitted to the Louisville City Hospital on March 14, 1934. The chief complaint was blackness and dryness of the left leg.

The infant was the first-born child of a 16 year old mother. The previous health of both parents had been good, and there was no history of diabetes in either of their families. During the last three months of her pregnancy, the mother had been troubled with nausea and vomiting and, according to her statement, "had eaten nothing but corn flakes and hot chocolate." At the time of delivery, she was ill with mumps.

The infant was delivered precipitately at term, the physician arriving at the home about ten minutes afterward. Labor was not unusually long or difficult, and there was no history of the cord's causing constriction anywhere. The weight at birth was estimated to be about 8 pounds (3,175 Gm.). The grandmother stated that the baby's feet were a little blue immediately after birth but that after they were bathed the color became normal. The infant took the breast poorly from birth and at the age of 9 days was put on a formula of whole milk 12 ounces (354.9 cc.), water 6 ounces (177.4 cc.) and corn syrup 1 ounce (29.6 cc.). This formula was taken better than the breast feeding, and the infant took water well.

When the child was 9 days old the family noticed that his face was becoming thin. Two days later a blue spot was noticed on the sole of the left foot; the

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discoloration spread upward to the midportion of the leg within a short time and then more gradually above the knee. Four days after the onset the leg began to look dry. There had been some tendency to constipation, and one of the first meconium stools was said to have contained blood. The infant vomited once, three days before admission. The cord dropped off at the end of seven days, and there was apparently no infection until two days before admission, when

Fig. 1.—Photograph of the patient.

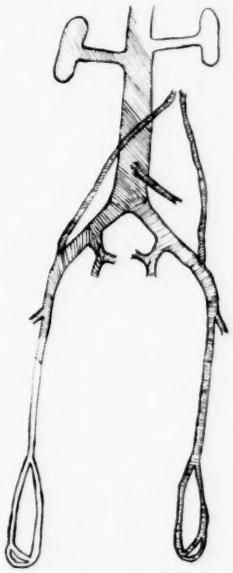

Fig. 2.—Diagram of the lower part of the aorta and of the kidneys and the large arteries. The shaded portion indicates the extent of the thrombosis.

some drainage occurred. The infant had had eight or nine slight generalized convulsions during the week preceding admission to the hospital.

On admission, the temperature was 105 F., rectally. The infant weighed 4 pounds and 11 ounces (2,126.2 Gm.) and was extremely emaciated and dehydrated. He appeared moribund but was not comatose, crying feebly when stimulated. The respirations were irregular, with short periods of apnea. The

anterior fontanel was deeply sunken. The heart beat was very rapid and somewhat irregular. The umbilicus was infected and oozing slightly. The left foot and leg showed dry gangrene extending above the knee, where there was a definite line of demarcation; the extremity felt cold. No pulsation could be felt over either femoral artery, although the right lower extremity looked normal. Figure 1 shows the patient several hours after admission.

The blood sugar content shortly after admission was 0.952 per cent. The value for plasma bicarbonate was 18 volumes per cent. The urine obtained two

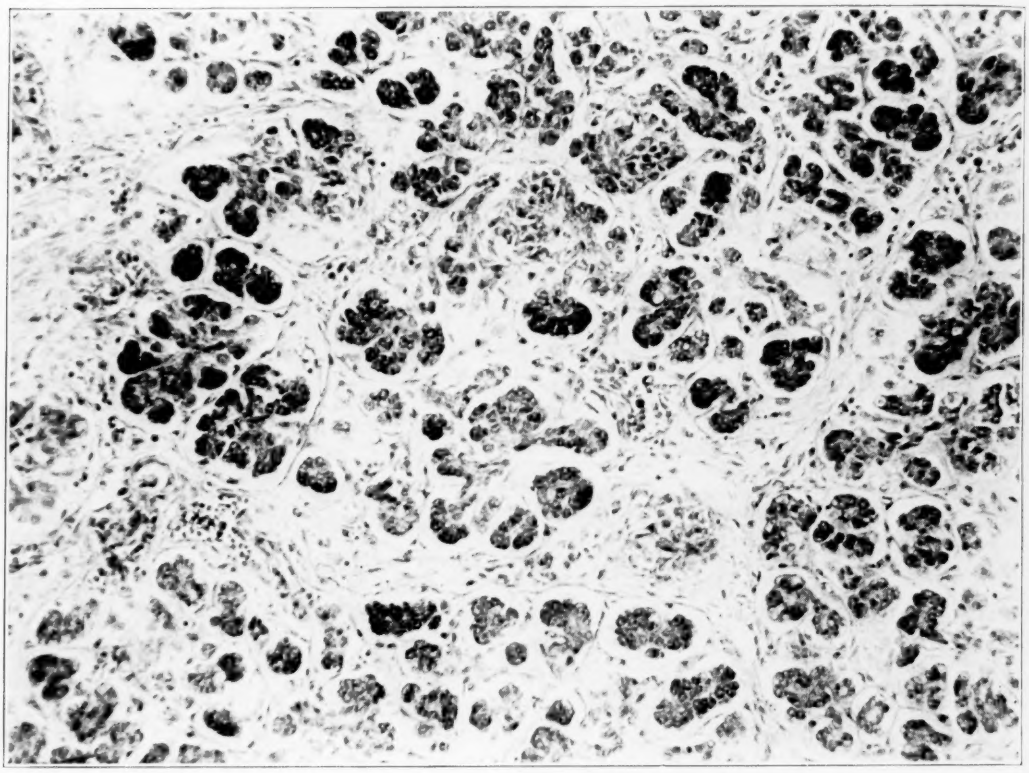

Fig. 3.—Photomicrograph showing marked acute degeneration of the islet cells. The cytoplasm contains vacuoles and large masses of dense material. The boundaries of the cell are not visible. Small groups of cells have died. There is no leukocytic infiltration.

hours later was red, cloudy and acid, but the quantity was not sufficient to determine specific gravity; examination showed albumin (3 plus); the test for sugar with Benedict's solution gave a heavy brick-red precipitate; the reaction for acetone was 1 plus, and many red blood cells were seen on microscopic examination. The white cell count of the blood was 38,000 per cubic millimeter. The Wassermann reaction was negative.

The patient entered the hospital at noon. Immediately after admission, the infant was given 200 cc. of lactate-Ringer solution subcutaneously, and small

amounts of water were given by nasal catheter; these were retained. At 3:15 p. m., 75 cc. of a 10 per cent solution of dextrose with 10 units of insulin was given intravenously, and 20 units of insulin, subcutaneously. A continuous venoclysis of a 5 per cent solution of dextrose was then started. At 6 p. m., the urinary reaction for sugar was still 4 plus, and the reaction for diacetic acid, negative. The blood sugar at that time was 0.22 per cent. At 8 p. m., the urinary reaction for sugar was again 4 plus, and the reaction for diacetic acid remained negative. At that time, the venoclysis had stopped running, and 60 cc.

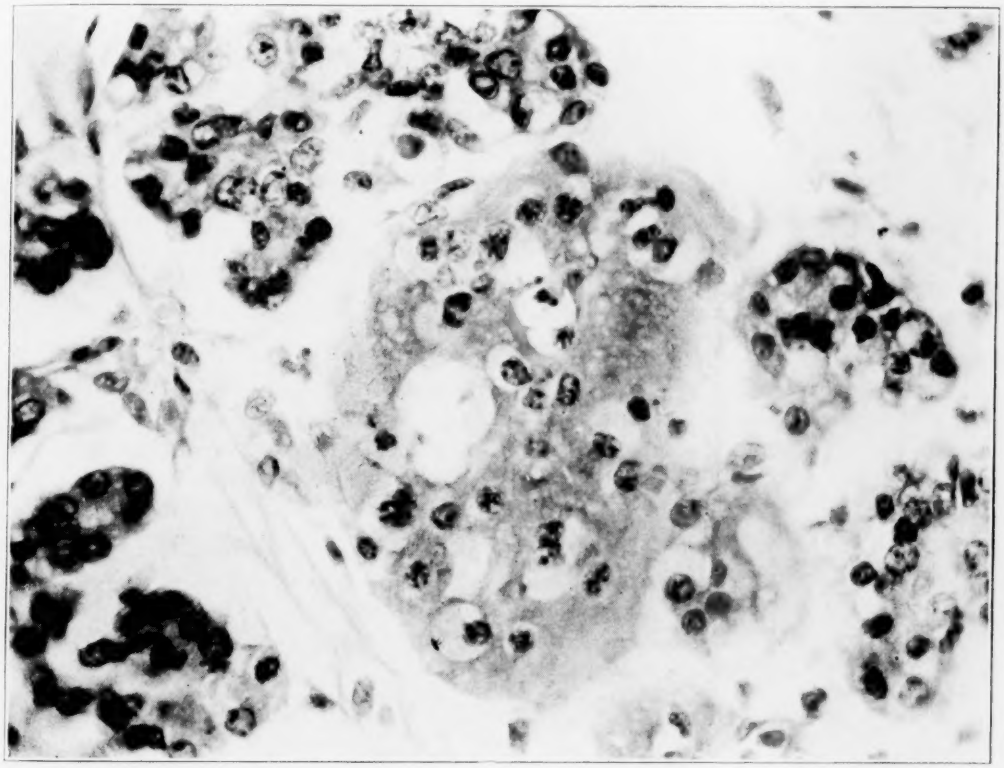

Fig. 4.—Photomicrograph showing much scarring of the stroma, including that of the islets. The islet cells are pyknotic and decreased in number. These changes are in the head portion only.

of a 10 per cent solution of dextrose was given by nasal tube, together with 6 units of insulin subcutaneously; at 10 p. m., 10 units of insulin was given.

The infant's temperature dropped to normal several hours after admission. He had one small constipated stool, and an enema was returned highly colored. He died quietly at 11 p. m. on the day of admission.

Necropsy was performed about fourteen hours after death.

The state of nutrition was poor. The left lower extremity was gangrenous from the junction of the middle and lower third of the thigh downward (fig. 1). The borderline of the gangrenous area was narrow and definite, but there was no separation of granulation tissue.

The umbilicus was crusted, but there was no swelling or discharge from it.

The aorta was occluded by a recently formed thrombus from just above the level of the right renal artery downward. The right kidney was black and completely infarcted. A small channel remained on the left side of the blood clot and extended into the left renal artery, so that the circulation was maintained to the left kidney, which was normal (fig. 2).

Just below the left renal artery there was complete occlusion of the aorta. This occlusion extended into all the branches of the aorta below the left renal artery. In the right lower extremity the femoral artery was occluded to the midportion of the thigh, beyond which the blood was liquid. On the left side the arteries of the lower extremity were all completely occluded. The hypogastric arteries on each side were completely occluded throughout their entire length.

Sections of the hypogastric arteries taken at the umbilicus contained infected thrombi and a mild inflammatory reaction in the walls as well as in the surrounding tissue. However, sections taken 1 cm. from the umbilicus showed no evidence of infection. There was no microscopic evidence of the thrombosis resulting from arteritis extending from the infected area along the arteries. There was slight variation in the age of the clot at different levels, but there was no indication of progressive formation. Sections of the clot near the kidney indicated that it was older here than in the right iliac artery.

No gross changes were noted in the organs of the chest and abdomen.

Microscopic study of the liver revealed a slight fatty infiltration, but no glycogenic degeneration. A few canaliculi were distended with bile.

Sections of the pancreas indicated the presence of an old pancreatitis of the head portion. The stroma was dense and increased. Many of the islets were scarred (fig. 3). In both the head and the tail portion there was questionable increase in the number of islets. In the tail portion there were moderate pyknosis, rather general acute degeneration and a very occasional small group of dead cells in the islets (fig. 4). There was no leukocytic infiltration. The cytoplasm of some of the islet cells contained large vacuoles.

The lungs were moderately edematous.

COMMENT

The damage found in the islet cells was sufficient to account for the hyperglycemia. However, the cause of the degeneration and of the fibrosis was not apparent. The possibility that the virus of mumps produced the pancreatitis found in the head of the pancreas is an interesting question for speculation. John cited the case observed by Barbieri,[1] in which the patient apparently had temporary diabetes following pancreatitis associated with mumps. The findings in the pancreas of our patient did not resemble the changes found in the parotid glands in mumps, and the involvement of the islets was more marked in the body and in the tail of the pancreas, where the acinar tissue was normal. The process in the islets appeared to be an acute degeneration, while the involvement of the acinar tissue of the head of the pancreas represented an old process, probably antedating birth.

1. Barbieri, V.: Gazz. d. osp. **30**:273, 1909; cited by John, H. J.: Ann. Int. Med. **8**:198 (Aug.) 1934.

The gangrene of the left leg and the infarcted right kidney were attributed to the thrombosis, but the cause of the extensive blood clot was not revealed. Microscopic study of the arteries did not indicate that it was secondary to arteritis progressing from the umbilicus. We cannot say whether the thrombosis preceded the onset of diabetes or whether the profound metabolic disturbance of diabetes, with dehydration and increased viscosity of the blood, led to the thrombosis. Thrombosis of the venous sinuses of the dura has been reported in acute nutritional disturbances with severe dehydration. Arterial thrombosis would seem to be more difficult to produce in this way. Very few cases of gangrene associated with diabetes in infancy and childhood have been reported, and, as far as we can ascertain, our case is the first one to be examined from the standpoint of pathology.

REVIEW OF THE LITERATURE

The first case to be reported as one of gangrene associated with diabetes in early infancy was that by Eaton and Woods (1911).[2] This infant did well until the age of 6 months, when there appeared swelling of the third toe of the left foot, with formation of vesicles. A week later, a similar lesion appeared on the fourth toe of the right foot. A month later, the condition of the toes was unchanged, and the mother noticed that the diapers were sticky. The urine showed a strongly positive reaction for sugar, a high specific gravity and a positive reaction for acetone. The glycosuria and swelling of the toes persisted, with gradual disappearance of the redness. The case was reported five months after the onset of the infant's illness, and, according to Knox,[3] the infant lived nineteen months longer. The lesions of the toes probably represented pregangrenous changes rather than true gangrene. In the case reported by Smith,[4] that of a 3 year old child observed in the Louisville City Hospital, there evidently was a similar process. In 1928, Joslin,[5] discussing the rarity of gangrene in juvenile diabetes, cited this case.

A second case of infantile diabetes with gangrene was that observed by Ashby (1923).[6] His patient was a girl who was admitted to the hospital at the age of 5 months because of pyelitis; the child had been irritable and hard to feed and had had frequent offensive stools all her life. Three weeks after admission gangrene developed in the second toe of the left foot. At that time the urine was found to contain sugar.

2. Eaton, P. J., and Woods, E. B.: Tr. Am. Pediat. Soc. **23**:244, 1911.
3. Knox, J. H. M., Jr.: Bull. Johns Hopkins Hosp. **24**:274 (Sept.) 1913.
4. Smith, T. C.: Kentucky M. J. **25**:425, 1927.
5. Joslin, E. P.: Treatment of Diabetes Mellitus, Philadelphia, Lea & Febiger, 1928.
6. Ashby, H.: Lancet **1**:22, 1923.

Two days later, gangrene of the second toe of the opposite foot developed; two weeks later, both toes came off. The patient died in coma three weeks after the onset of the gangrenous condition.

A third case was reported by Lawrence and McCance [7] in 1931. The patient, a girl, was found to have a black patch on the right wrist on the fifteenth day of life; on the seventeenth day a similar spot developed on the left ankle. The following day a spot appeared over the right trochanter, over a pressure point. The infant had lost over 2 pounds (907.18 Gm.) during the six days prior to entering the hospital at the age of 18 days. On the nineteenth day of life a spot appeared over the left trochanter. The urine contained 4.2 per cent sugar, albumin and no acetone. The blood sugar was approximately 0.6 per cent. Insulin was given for six days, and the infant recovered from the glycosuria. The gangrenous areas over the hips separated and finally healed.

In 1931 Strandqvist [8] published the report of a case very similar to that observed by Lawrence and McCance and presented the criteria which the latter had laid down for a diagnosis of diabetes mellitus in infancy. We feel that the case should be included in this series. According to Strandqvist, the patient was a boy in whose family history there was no evidence of diabetes. When he was 6 weeks old an area of reddish swelling appeared on the right shoulder, together with fever and thirst; the area became fluctuant and was incised and drained. Almen's test for sugar was positive on the patient's admission to the hospital, and a later quantitative examination showed 8 per cent. Tests for acetone and aceto-acetic acid gave negative results. The blood sugar the day after admission was 0.42 per cent. The edges of the abscess became gangrenous. The infant was treated for two weeks with small doses of insulin, and he recovered, the values for urinary and blood sugar gradually dropping. Following recovery, a test for dextrose tolerance gave normal results.

Accompanying their case report in 1931, Lawrence and McCance [7] published a critical review of cases of diabetes with the onset prior to the age of 1 year. In their review, they accepted the diagnosis of infantile diabetes as proved in cases in which (1) definite wasting, thirst, polyuria and preferably ketonuria were present, accompanied by extreme glycosuria (sugar content over 2 per cent), whether the reducing substance was actually proved to be dextrose or not and even if hyperglycemia was not established, or (2) if the symptoms of glycosuria were slight but definite and recurrent hyperglycemia (sugar content over 0.2 per cent) was established.

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7. Lawrence, R. D., and McCance, R. A.: Arch. Dis. Childhood **6**:343, 1931.
8. Strandqvist, B.: Infantile Glycosuria Simulating Diabetes, Acta pædiat. **13**:421, 1932.

In this country, Knox [3] collected fifteen cases of diabetes with onset prior to the age of 1 year, which were reported up to 1913, and added one of his own. Lawrence excluded the case observed by Caillot, which was included in the earlier series, and regarded as doubtful cases one reported by Garnerus and two by Langstein. He added to the earlier cases that of Haüner (1850), which he regarded as the first authentic instance of diabetes in an infant less than a year old, and those of Baumel (doubtful), Lauritzen and Cuño, and he brought the collection up to date with twelve additional cases, including his own. White [9] in 1931 accepted the combined collections of Knox and Lawrence, with a total of thirty-two cases, and mentioned three additional cases observed by White and by Joslin; these have not as yet been reported in detail. We are including among the earlier cases that of Hartmann (1925),[10] and we have added four cases reports of which have appeared in the literature since 1931—that of Strandqvist (1932),[8] reviewed earlier in this paper; that of Nyström (1932);[11] that of Newcomb (1934),[12] which is incompletely reported; and one reported by Lewis and Eisenberg (1935).[13] This brings the total to forty, not including our own case.

Recently, John [14] published a table of seventy-eight cases of diabetes with the onset prior to the age of 1 year. This collection does not include the case reported by Lawrence and McCance or the five cases just referred to; we believe, however, that the number is much too high. Since the author did not give dates or references, we were unable to investigate all of these cases; there are, however, several apparent inaccuracies. As diabetes in cases of new-born infants, John listed the cases observed by LaSalle, Morrison, Ambard, Feldman, Osler and Schretter and Nevinny. We are not familiar with LaSalle's case. The reference in Morrison's [15] statistical study of deaths from diabetes in Boston (1916) is as follows: "The youngest case reported as having died from diabetes was that of a newly-born infant taken from a diabetic mother, who also succumbed." Ambard [16] reported diabetes in a premature infant whose diabetic mother was moribund at the time of delivery. The sugar content of blood from the cord was 0.242 per

9. White, Priscilla: Diabetes in Childhood and Adolescence, Philadelphia, Lea & Febiger, 1932.

10. Hartmann, A. F.: M. Clin. North America **9**:69 (July) 1925.

11. Nyström, G.: Svenska läk.-tidning. **29**:1265 (Nov. 25) 1932.

12. Newcomb, A. L.: J. Pediat. **4**:617, 1934.

13. Lewis, E., and Eisenberg, H.: Diabetes Mellitus Neonatorum: Report of a Probable Case, Am. J. Dis. Child. **49**:408 (Feb.) 1935.

14. John, H. J.: J. Pediat. **6**:211, 1935.

15. Morrison, H.: Boston M. & S. J. **175**:54, 1916.

16. Ambard, L., et al.: Bull. et mém. Soc. méd. d. hóp. de Paris **49**:547, 1925.

cent and that of the mother's blood was 0.193 per cent. The infant showed sugar in one specimen of urine and lived only a short time; autopsy revealed cirrhosis and lymphocytic infiltration of the acinar tissue of the pancreas, with normal islets. A determination of the sugar content of the infant's blood was not made, and while the data suggest diabetes, they are not conclusive. Feldman [17] reported a "case" which has been cited several times as one of congenital diabetes in an unborn fetus of a mother dying in diabetic coma; the pathologic condition found in the islands of Langerhans is interesting, but this is not a clinical case. The reference given by Osler [18] was very casual; he stated that "one case is mentioned of a child apparently born with glycosuria, who recovered in eight months." This is probably not the author's own case, but no reference is given. Schretter and Nevinny [19] regarded as diabetic the infant of a diabetic mother; the child showed normal blood sugar at birth and an increasing but moderate hyperglycemia up to the time of its death at the age of 32 days. Death was due to congenital cardiac disease, and there was no glycosuria or symptoms of diabetes. Autopsy showed, in addition to several congenital defects of the heart, only hypertrophy of the islands of Langerhans, a finding not uncommon in the offspring of diabetic mothers. Lawrence regarded the hyperglycemia as probably associated with circulatory failure and cyanosis, since asphyxia elevates the blood sugar.

The case observed by Caron [20] and included in John's table was that of a 3 months old infant who had only slight glycosuria without symptoms of diabetes. In his case, that of a 10 month old infant, Burghard [21] did not diagnose the condition as diabetes but as "pancreatic disease." In view of the microscopic observation of cystic degeneration of the pancreas with increase in the interstitial tissue, the author assumed that some of the patient's symptoms might have been due to impairment of the function of the islands of Langerhans. There was no glycosuria, and a determination of the blood sugar was not made.

The apparent duplications in John's table are: Three cases are credited to Dreyfuss, Nichues and Hagenbach and also to Wegeli,[22] who reviewed them; Stern [23] is given credit for six cases reviewed by him, four of which are credited separately to Busch, Rossbach, Kitselle and Garnerus. (The data given by Stern on the cases of Rosenbach, Jacoby

17. Feldman, I.: Centralbl. f. allg. Path. u. path. Anat. **42**:435, 1928.

18. Osler, W.: Principles and Practice of Medicine, ed. 10, New York, D. Appleton & Company, 1925.

19. Schretter, G., and Nevinny, H.: Arch. f. Gynäk. **143**:465, 1930.

20. Caron, cited by Wegeli.[22]

21. Burghard, E.: Klin. Wchnschr. **4**:2305 (Nov. 26) 1925.

22. Wegeli, E.: Arch. f. Kinderh. **19**:1, 1895.

23. Stern: Arch. f. Kinderh. **11**:81, 1890.

and Griesinger and Wegeli's data on the case reported by Dreyfuss are inadequate for a diagnosis of diabetes.) We found reports of one case by each of the following authors: Kochmann,[24] Lenstrop,[25] Knox,[3] Schippers[26] and Shelley;[27] John listed two cases for each of them. DeLange,[28] who reported the microscopic observations in Schipper's case and reviewed the pathologic observations in Kochmann's case, is also given credit for two cases. Heiberg[29] is credited with three cases, two in infants under 1 year and one in an infant 90 days old. One is an authentic instance of diabetes, but the child was 15 months old; the second case was that of an infant of the same age not having diabetes, on whom the islands of Langerhans were studied for comparative purposes; the condition of the infant 90 days old was diagnosed as "glycosuria" by the author. The highest percentage of sugar in the urine was 1.5; there was no acetonuria, and the infant died of bronchopneumonia. There was no determination of the blood sugar, and microscopic examination of the islands of Langerhans showed no qualitative change.

There will probably always be some difference of opinion concerning the earlier cases. It is highly desirable, however, that observers reporting cases in the current literature give all the available data. In the following tabulation we submit our collection of cases from the literature. We attempted to summarize the various aspects of the disease as they occurred in the collected cases. Many of these cases are included in Lawrence and McCance's[7] collection, and readers are referred to this work for abstracts of the cases. In order to make it available in the American literature, the case observed by Nyström[11] is summarized.

The patient was an 11 month old girl whose illness began suddenly a few days before admission to the hospital with unusual thirst and loss of weight. Within a short time she became weak, pale and apathetic and began vomiting; on the morning of the day of admission she became comatose. Her previous health had been good. She was breast fed, and during the last two months this feeding had been supplemented by the family diet. (Nyström seemed to regard this diet as high in carbohydrate and commented on the high incidence of diabetes in this community, particularly among children.) There was no family history of diabetes; three siblings had died in infancy, two of unknown diseases. Examination of the patient on admission to the hospital showed deep coma, dehydration,

24. Kochmann, R.: Jahrb. f. Kinderh. **99**:20, 1922.

25. Lenstrop, E.: Klin. Wchnschr. **8**:2244, 1929.

26. Schippers, J. C.: Diabetes Mellitus in an Infant Aged Eight Months Treated with Insulin, Am. J. Dis. Child. **30**:336 (Sept.) 1925; Nederl. tijdschr. v. geneesk. **1**:2206, 1905; cited by White.[9]

27. Shelley, E. G.: Pennsylvania M. J. **34**:256, 1931.

28. DeLange, C.: Morbid Anatomy in a Case of Diabetes, with Onset at the Age of Eight Months, Am. J. Dis. Child. **31**:840 (June) 1926.

29. Heiberg, K. A.: Arch. f. Kinderh. **56**:403, 1911.

Observer	Year	Age at Onset	Outcome
Haüner [30]	1850	11 months	Died in coma
Kitselle [31]	1852	A few days	Died after 6 months
Rossbach [32]	1874	7 months	Died after 3 months
Busch [33]	1876	"Under a year"	Died in coma
Hagenbach [34]	1879	8 months	Died after 11 months
Garnerus [35]	1884	2 months	Recovered
Nichues [36]	1891	3 months	Died
Tavaria [37]	1893	10 months	Died in coma
Bell [38]	1896	2 months	Died in coma
Baumel [39]	1900	6 months	Recovered
Caillot [40]	1900	5 months	Recovered
Orloff [41]	1901	5 months	Died
Young [42]	1902	6 months	Died after 1 month
Langstein [43]	1909	6 months	Died
Langstein [43]	1909	7 days	Died
Langstein [43]	1909	8 months	Ultimate fate not recorded
Lauritzen [44]	1910	8 months	Died in coma
Eaton and Woods [2]	1911	6 months	Died after 2 years (Knox)
Cuño [45]	1911	15 days	Died
Knox [3]	1913	8 months	Died in coma
Kochmann [24]	1922	4½ months	Died in coma
Ashby [6]	1923	5 months	Died in coma
Hartmann [10]	1925	12 months	Doing well on insulin
Major and Curran [46]	1925	6 months	Doing well on insulin
Schippers [26]	1925	8 months	Died after 18 months
Arndt and Welcker [47]	1926	3 months	Died (cardiac failure ?)
Ramsey [48]	1927	4 weeks	Recovered after 18 days on insulin
Morton [49]	1928	12 months	Doing well on insulin 1 year after onset
Joslin [5]	1928	8 months	Doing well on insulin
Lenstrop [25]	1929	12 months	Died in coma
Litchfield and Shermer [50]	1930	5 months	Doing well on insulin
Shelley [28]	1931	8 months	Died after 7 months
Lawrence and McCance [7]	1931	15 days	Recovered on insulin
White [9]	1931	?	One patient died; two doing well on insulin
Nyström [11]	1932	11 months	Died after 1 month
Strandqvist [8]	1932	6 weeks	Recovered on insulin
Newcomb [12]	1934	10 months	Died after 12 days
Lewis and Eisenberg [13]	1935	9 days	Died of infection
Limper and Miller	1935	9 days	Died

30. Haüner: Wchnschr. f. d. ges. Heilk. **21**:321, 1850.

31. Kitselle: J. f. Kinderh. **18**:313, 1852; cited by Stern.[23]

32. Rossbach, T.: Berl. klin. Wchnschr. **2**:258, 1874.

33. Busch: Jahresb. u. d. Fortschr. d. ges. Med. **2**:271, 1876; cited by Stern.[3]

34. Hagenbach: Jahrb. f. Kinderh. **13**:421, 1879.

35. Garnerus, H.: Deutsche med. Wchnschr. **10**:697, 1884.

36. Nichues, F., cited by Wegeli.[22]

37. Tavaria, H. K.: Indian Med.-Chir. Rev. **1**:402, 1893; cited by Lawrence and McCance.[7]

38. Bell, W. B.: Edinburgh M. J. **41**:709, 1896.

39. Baumel, M. L.: Compt. rend. cong. internat. de méd., Paris, 1900, p. 627; cited by Lawrence and McCance.[7]

40. Caillot, cited by Knox.[3]

41. Orloff, M. N.: Semaine méd. **21**:192, 1901; cited by Lawrence and McCance.[7]

42. Young, W. E.: Arch. Pediat. **18**:198, 1901.

43. Langstein, L.: Verhandl. d. Kong. f. inn. Med. **26**:209, 1909; cited by Knox.[3]

44. Lauritzen, M.: Arch. de méd. d. enf. **13**:561, 1910.

45. Cuño, F.: Klin.-therap. Wchnschr. **18**:57, 1911; Ztschr. f. Kinderh. (Ref.) **1**:191, 1912.

46. Major, R. H., and Curran, E. J.: Diabetic Cataracts in an Infant, J. A. M. A. **84**:674 (Feb. 28) 1925.

47. Arndt, H. J., and Welcker, A.: Ztschr. f. Kinderh. **41**:518, 1926.

48. Ramsey, W. R.: Tr. Am. Pediat. Soc. **38**:100, 1926.

49. Morton, H. B.: Nebraska M. J. **13**:9, 1928.

50. Litchfield, H. R., and Shermer, B.: Pediatric Bull. **1**:5 (Oct.) 1930; cited by White.[9]

muscle atony, soft eyeballs, a rapid, weak pulse and a subnormal temperature; no evidence of infection was discovered. The urine gave a positive reaction to Almen's test for dextrose. The first determination of the blood sugar, made several hours after administration of insulin, showed 0.175 per cent. Subsequent determinations of blood sugar showed from 0.254 to 0.392 per cent, although the urine remained sugar-free most of the time with doses of from 7 to 10 units of insulin daily. The patient's condition did not improve on the regimen of diet and insulin, and after several days of increased weakness and vomiting, she died, about one month after the onset of her illness; the urine was sugar-free at the time of death. Autopsy was performed, and the only gross pathologic condition found was bilateral basal bronchopneumonia. The results of microscopic examination of the pancreas were reported as follows: "Islands of Langerhans, few and small; necrosis here and there in the remaining parenchyma."

COMMENT ON THE COLLECTED CASES

Symptomatology.—The infants with diabetes, in common with most patients in the younger age group, had a comparatively acute onset. Excessive thirst and polyuria, fairly frequent symptoms in older children with diabetes, were noticed quite constantly in the infantile group. Loss of weight was usually observed, and many of the patients were noted to be quite emaciated when first brought for consultation. Other complaints were restlessness, fever, intertrigo and sticky diapers. Many of the patients had infections when first seen. Edema and severe anemia were observed in the case reported by Arndt and Welcker,[49] and edema alone was present in those observed by Caillot[40] and Baumel.[39]

As complications, gangrene or pregangrenous changes appeared in the four cases reviewed by the authors just mentioned, and gangrene of the lung was seen at autopsy in Hagenbach's[34] case. A true diabetic cataract was reported once, in a 6 month old patient observed by Major and Curran.[46]

Incidence.—Of the cases in which the infant's sex was mentioned, twenty-one were in boys, and ten in girls, giving an incidence of 67.7 per cent in boys. The age incidence in the cases in which the age was given is as follows: Ten occurred in infants under 3 months; seven, from 3 to 6 months; seven, from 6 to 9 months, and ten, from 9 to 12 months. Two of the infants, the one observed by Lewis and Eisenberg[13] and our patient, were Negroes. Tavaria[37] reported a case in a Parsee Indian child. In this series, no unusual incidence in the Jewish race was noted.

Etiology.—A definite statement as to the family history was made in twenty-one cases; eight patients, or 38 per cent, had a family history of diabetes. This is a rather striking incidence, since most of these patients were observed for short periods only and, as White[9] has pointed out, the longer juvenile patients are observed, the greater the number of additional cases found in their families.

The most important precipitating factor seems to have been infection; this preceded or accompanied the onset of diabetes in about 40 per cent of the cases. John [51] found that in 21 per cent of his cases in children the onset was within sixty days after an acute infection. Toverud [52] pointed out that 26 per cent of her cases in children developed within six weeks after an infection, and she regarded infection as more important than heredity in the development of juvenile diabetes. In the older literature, considerable significance was attached to neurologic lesions as etiologic factors in this disease. One of Langstein's [43] doubtful cases was in an anencephalic monster, and the other in a patient with hydrocephalus; hydrocephalus was also present in Hagenbach's [34] and Orloff's [41] cases. In Rossbach's [32] case, symptoms dated back definitely to cerebral concussion sustained in a severe fall on the head one month before the diagnosis of diabetes was made. Overfeeding with carbohydrates is suggested in the cases reported by Nichues,[36] Knox,[3] Morton [49] and Nyström.[11]

Pathologic Condition.—Significant pathologic changes in the pancreas have been found in some of the cases in which autopsy was performed. In Cuño's [45] case (not proved to be one of diabetes) there was a small pancreas, with cirrhosis of the interstitial tissues but with normal islets. Kochmann [24] reported proliferation of the connective tissue of the pancreas in his case, with decrease in the number of islets; there was also fatty degeneration of the liver. DeLange [28] found some decrease in the size of the pancreas in the case observed by Schippers, with normal islets. There were also fatty degeneration of the liver and some suggestion of a pathologic condition in the thyroid, adrenals and ovaries. Knox [3] reported round cell infiltration of the interstitial tissue of the pancreas and diminution in the size and number of islets. Heiberg [29] described some round cell infiltration in the islets and surrounding interstitial tissue in an infant 15 months old. Arndt and Welcker [47] found fatty infiltration of the acinar tissue of the pancreas, with very slight round cell infiltration of the islets; there were marked fatty degeneration of the liver, hemosiderosis of the spleen, sclerotic atrophy of the thymus and fatty infiltration of the adrenals. In Lenstrop's [25] case there was atrophy of the interstitial tissue, with "reduction in number and poor development" of the islands of Langerhans; fatty degeneration of the liver was also noted in this case. The pathologic condition in Nyström's [11] case has been given previously. Lewis and Eisenberg [13] found an increased amount of interacinar fibrous tissue and a reduction in the number of islets. Newcomb [12] found gross atrophy of the pancreas in his case, without any microscopic changes.

51. John, H. J.: Ann. Int. Med. **8**:198 (Aug.) 1934.
52. Toverud: Brit. J. Child. Dis. **24**:185, 1927.

With regard to the gangrene and pregangrenous changes in their own case and in those of Eaton and Woods and of Ashby, Lawrence and McCance [7] stated: "In older children and young adults these signs are practically unknown and in elderly diabetics are essentially due to concomitant arterial degeneration. In infants it must be presumed that the nutritional disturbance of severe diabetes, acute in our case, may produce gangrene apart from arterial disease."

Treatment.—Treatment of the older patients usually consisted of an attempt to control the glycosuria by diet alone, though various medications were tried also; it is rather surprising that some of the patients lived for considerable periods on such regimens. Since 1925, all the patients have received insulin along with dietary control. Insulin reactions are rather frequent in this age group, and several observers found that it was not possible to keep the urine consistently sugar-free for this reason. The amounts of insulin used were quite variable, and the small doses necessary to control the glycosuria in several of the cases suggest that the infants had mild diabetes. White [9] and Joslin [5] recommended a diet very similar to that for the average normal infant of the same age, with sufficient insulin to control glycosuria and hyperglycemia. Joslin commented on the comparative simplicity of the dietetic management in this age group; problems of discipline are also less frequent in the infant than in older children. Protecting these infants from infection by avoidance of contact as far as possible and by immunization when specific prophylaxis is available is of the utmost importance. In the presence of infection, the most careful handling is necessary, not only to guard against the immediate danger of severe acidosis but to protect against permanent reduction in the infant's carbohydrate tolerance. Carbohydrate should be supplied freely, with sufficient insulin to insure its assimilation; the intake of fluids must be adequate; and the infection itself should be skilfully cared for.

Prognosis.—The prognosis of diabetes in infancy depends mainly on how soon the case comes to the attention of the physician, on intelligent control in the home and on prompt and skilful handling of emergencies by the physician. The age at onset seems to be of some significance also, since no patient who acquired permanent diabetes under 3 months of age survived; and only two patients with the onset at the age of 5 and 6 months, respectively, were alive when their cases were reported—those observed by Litchfield and Shermer [50] and Major and Curran.[46] In the preinsulin era, the patient surviving longest was the one reported by Eaton and Woods [2] as living for two years after the diagnosis was established. Of the nineteen patients whose cases were reported in the insulin era, nine have died. Schippers had a little difficulty in controlling his patient because of a behavior problem, when he first reported the case; the child had a positive reaction to tuberculin

when first seen and died of bronchopneumonia eighteen months after the onset of diabetes. Shelley's [27] patient returned to a rural community after the initial observation and died of an acute intestinal infection seven months after the diagnosis was made. Arndt and Welcker's [49] patient was under observation for seven days and received insulin on the last day only; the patient was edematous and anemic when admitted, and ten hours after the injection of insulin the edema suddenly increased, and the infant died with symptoms of cardiac failure. In Nyström's [11] case the patient was in coma when first seen and succumbed to bronchopneumonia one month after the onset of the illness; the urine was sugar-free at the time of death. One of the three patients mentioned by White [9] died; details were not given. Newcomb's [12] patient succumbed to multiple infections, having been kept sugar-free during most of the twelve days of observation. Lewis and Eisenberg's [13] patient was under observation only eight days and died from infection. Our own patient was moribund when first seen.

Of especial interest are the patients reported to have recovered from diabetes. Garnerus,[35] Baumel [39] and Caillot [40] reported cases all of which are rather doubtful and are not patricularly significant; however, the cases observed by Ramsey,[49] Lawrence and McCance [7] and Strandqvist [8] were all thoroughly studied and fully reported, and there can be little doubt that the patients actually had "temporary diabetes mellitus." Ramsey's patient had a family history of diabetes. All three patients were less than a month old, all had infections and all were treated with insulin. This seems to corroborate John's [52] statement that "protection of the organism during infections is very important, since in the early stages of diabetes, the process is to a certain extent reversible."

SUMMARY

A case of diabetes mellitus with onset at the age of 9 days is presented. Clinically, there was dry gangrene involving the left lower extremity to the midportion of the thigh. At autopsy, this was accounted for by thrombosis which involved the aorta and extended into all its branches from the level of the left renal artery downward. Examination of the pancreas showed pancreatitis involving the head of the pancreas and acute degeneration of the islands of Langerhans in the body and tail. The mother of this infant had mumps at the time of delivery, and the possibility of the pancreatitis being due to the virus of mumps is discussed.

Four case reports of gangrene associated with infantile diabetes are described. The literature on diabetes with onset prior to the age of 1 year is reviewed. Attention is called to the existence of temporary diabetes mellitus in patients in this age group.

Pediatric Biographies

DAVID BRIDGE LEES
1846-1915

A NOTE ON THE HISTORY OF CROWING RESPIRATION

JOHN RUHRÄH, M.D.†
BALTIMORE

David Bridge Lees was born in Manchester, England, in 1846 and was educated at Owens College in Manchester and Trinity College at Cambridge. He studied medicine at Guy's Hospital and did some postgraduate work in Vienna. He was a brilliant student at Trinity; he graduated in mathematics at 20 as second Wrangler and in addition took first prize in Greek and divinity. After studying at Guy's Hospital, he qualified as a member of the Royal College of Surgeons and took his medical degree at Cambridge in 1874. He spent a short time in educational work at Owens College but in 1875 he became a member of the Royal College of Physicians and in 1876 he secured the degree of Doctor of Medicine at Cambridge. In 1879 he was assistant physician at the Great Ormond Street Hospital for Sick Children, and in 1880 he was made assistant physician to St. Mary's Hospital.

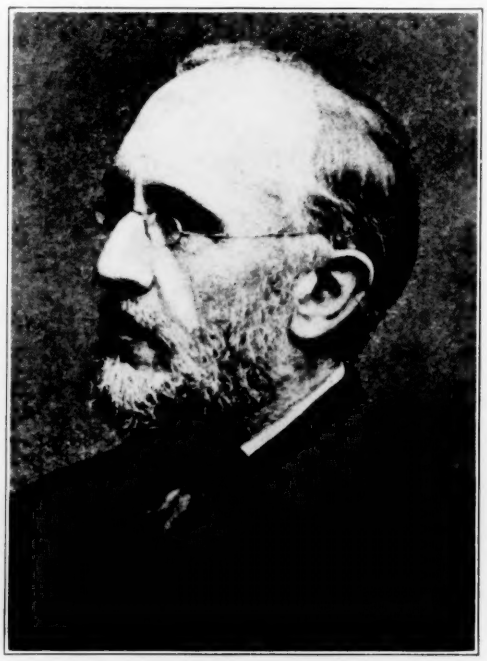
Lees was a specialist, but he paid particular attention to tuberculosis, rheumatism and heart disease, on which subject he wrote considerably. He was at one time president of the Harveian Society of London. He also paid special attention to the diseases of children, and his favorite treatment for acute rheumatism was enormous doses of sodium salicylate. He maintained that children require proportionately larger doses than grown-ups, as the disease is more intense in young people.

With Sir Thomas Barlow he contributed the article on "Simple Meningitis in Children" to Sir Clifford Allbutt's "System of Medicine" and the article on "Acute and Subacute Rheumatism" to Allchin's "Manual of Medicine." In 1912 he delivered the Bradshaw lectures of the College of Physicians on the signs, symptoms and treatment of incipient pulmonary phthisis, and in 1915 he was elected senior censor of the College of Physicians. In 1890 he was made a full physician to the Great Ormond Street Hospital, and in 1905 he was placed on the con-

† Deceased.

sulting staff. He was a very conscientious, religious man of a very retiring disposition and mixed little with his colleagues. He died in 1915.

He was particularly known as an investigator of diseases of children and was one of the first, if not the first, to recognize the cause of crowing respiration in infants. His account of this, which is dated Dec. 5, 1882, appeared in the *Transactions of the Pathological Society of London.*[1]



DAVID B. LEES
1846-1915

LARYNX FROM AN INFANT WHICH HAD BEEN THE SUBJECT OF A PECULIAR FORM OF OBSTRUCTED INSPIRATION

By David B. Lees, M.D.

The larynx now exhibited to the Society was taken from an infant of a year old, which had, during its whole life, manifested a peculiar noisy respiration. Each inspiration was accompanied by a croaking sound, whilst expiration was much less affected (indeed, usually entirely free) and the cry-sound was quite clear. About a month before the child's death a laryngoscopic examination was made, and it was then seen that the upper aperture of the larynx was in the form

1. Lees, D. B.: Tr. Path. Soc. London **34**:19, 1882.

of a narrow median slit, extending from above downwards, the epiglottis being folded on itself, so that the posterior surfaces of its lateral halves were almost in contact, and the ary-epiglottis folds close together and almost overlapping. A second examination was attempted a month later, when it was observed that a small white diphtheritic patch was present on each tonsil. The child died three days after this. The drawing shows the condition of the larynx as seen about two days after death.

The epiglottis is much curled inwards, even more than it usually is in infants. The aryteno-epiglottic folds are in close proximity (Woodcut 1); indeed, they seem to be in actual contact. They were quite thin and not at all oedematous when the specimen was obtained. Above them, below the centre of the folded epiglottis, is an opening of the size of a pinhole; and below them, between the arytenoid cartilages, a second and rather larger opening. The vocal cords and the rest of the interior of the larynx were healthy. The trachea was lined with diphtheritic membrane.

I have seen four cases in which this peculiar croaking inspiration was present. All four were girls. In all the condition appeared to be congenital, and in all fairly constant, except that occasionally exacerbations seemed to be caused by exposure to cold and by flatulence. The croak is of a lower pitch than the crow of laryngismus. It continues, though less loud, during sleep, and after the administration of chloroform. There is usually some recession above the sternum during inspiration, and slightly also at the base of the thorax; but as a rule sufficient air seems to enter the chest.

In at least one of the cases the symptom entirely passed away as the child grew. This is, I believe, the first time that the cause of obstruction has been ascertained either by the laryngoscope or by *post-mortem* examination.

Pediatrics in Art

MOTHER AND NURSING CHILD

JOHN RUHRÄH, M.D.†
BALTIMORE

There have been thousands of Madonnas with the Child but few more beautiful than the one shown in the illustration, which is known as the Madonna Litta and is in the Hermitage Collection in Leningrad,

Leonardo da Vinci's Madonna Litta.

U. S. S. R. The clothing is of particular interest, the head dress, the gown and the cloak being fine examples of the beautiful garments of the period. The painting is by Leonardo da Vinci, who, despite some authorities to the contrary, produced some of the most glorious art which has been seen in the artistic country of Italy. From a pediatric standpoint, the thing of especial interest is the nursing gown with the openings to permit the use of the breast without undressing or opening the clothing. A sensible design unfortunately rarely used today. Maybe if it were made the fashion more American mothers would nurse their babies.

† Deceased.

Obituaries

MORGAN SMITH, M.D.

1868-1935

Dr. Morgan Smith, of Little Rock, Ark., died on Sept. 14, 1935. Dr. Smith graduated from Tulane University in 1904 and has been engaged in the practice of pediatrics in Little Rock ever since. For many years he has been professor of pediatrics at the University of Arkansas, but this tells little of his usefulness to his state and his region.

Dr. Smith was looked on as an outstanding man from many angles. He served in the state legislature for several terms and was unquestionably the leading man in pediatric activities in Arkansas. In his death American pediatrics has lost a diligent worker and an outstanding character.

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HOYER, Cincinnati.

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The reaction obtained when these rabbits were tested later suggest that the toxin alters the antigenicity of lens and rabbit muscle and produces precipitins for low extract of ragweed. The rabbits became sensitive to the lens substance and rabbit muscle, so that slight trauma to the lens or muscle caused a marked reaction. A similar anaphylactic reaction was produced in the rabbits when they were exposed to the ragweed pollen.

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STOESSER, Minneapolis.

ISOLATION OF AN OBLIGATELY ANAEROBIC BACILLUS FROM THE FECES OF NEWBORN INFANTS AND FROM OTHER HUMAN SOURCES, AND ITS PROBABLE IDENTITY WITH THE "KÖPFCHENBAKTERIEN" OF ESCHERICH, RODELLA'S "BACILLUS III" AND BACILLUS PARAPUTRIFICUS (BIENSTOCK). IVAN C. HALL and M. L. SNYDER, J. Bact. **28**:181 (Aug.) 1934.

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These experiments not only increase the possibilities of developing a potent serum which will give passive immunization to human beings, but indicate that the difference between the European virus and the Mexican virus is much less fundamental than has been supposed, and that it is not impossible that it depends largely on minor modifications sustained in the course of passage of the Mexican, so-called New World virus through rats and the fleas of rats.

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News and Comment

GENERAL

Bequests and Donations.—The following bequests and donations have recently been made: St. Agnes' Hospital for Crippled Children, White Plains, N. Y., $18,000 by the will of Walter G. Butler; Shriners' Hospital for Crippled Children, Philadelphia, $12,000, by the will of the late Marie Redifer, Atlantic City, N. J.; New York Orthopaedic Dispensary and Hospital, $10,000 by the will of Mrs. Harriet Crocker Alexander, and St. Luke's and Children's Hospital, Philadelphia, $10,000 by the will of the late Mrs. Elizabeth Powell. The Children's Medical Division of Bellevue Hospital, New York, will ultimately receive most of the estate of Mrs. Anna Phipps Tinker, widow of the late Dr. Horace H. Tinker. The estate was appraised at about $250,000.

United States Civil Service Examinations for Public Health Consultants.—Applications for various grades of public health consultants and for a public health research assistant must be on file with the United States Civil Service Commission, Washington, D. C., not later than Nov. 25, 1935.

Optional subjects for the positions of consultant are: maternal and child health, general public health practice and orthopedics. The specialty for the research assistant is maternal and child health.

Entrance salaries for the positions of consultants range from $2,600 to $4,600 a year. The entrance salary for the research assistant is $2,000 a year. These salaries are subject to a deduction of 3½ per cent toward a retirement annuity.

Vacancies in these positions in the Children's Bureau, the Department of Labor, and in the United States Public Health Service, the Treasury Department, both in Washington, D. C., and in the field, will be filled from these examinations. Certain education and experience are required. Full information may be obtained from the Secretary of the United States Civil Service Board of Examiners at the postoffice or custom-house in any city which has a postoffice of the first or second class or from the United States Civil Service Commission, Washington, D. C.

DEATHS

Luis Morquio of Montevideo, Uruguay, died on July 9, 1935. Dr. Morquio was one of the outstanding figures in pediatrics and probably the best known of the South American pediatricians. He described a bone disease, congenital in origin, which is known by his name. He was most active in the development of pediatrics and child welfare in his own country, being a founder of the *Archives de Pediatria del Uruguay* and other publications. Pediatrics has suffered a severe loss in the death of this outstanding pediatrician and teacher.

Abstracts from Current Literature

Anatomy and Physiology

SOME PROBLEMS IN THE GROWTH AND DEVELOPMENTAL MECHANICS OF BONE. JAMES BRASH, Edinburgh M. J. **41**:305 (May); 323 (June) 1934.

This is the sixth Sir John Struthers Lecture and was given before the Royal College of Surgeons in Edinburgh in 1933. It begins in the May issue and is concluded in the June number of the journal.

By vital staining Brash has shown experimentally that all changes due to growth in the size and form of individual bones occur through the process of accretion and absorption at surfaces. He gives in detail the processes at work in the development of various bones. In the case of individual bones, as, for instance the jaws, there are special accretion and absorption mechanisms relating to the tooth-bearing function. This is because of the essential necessity for continuous movement of teeth to retain their relative position in the jaw and their position relative to the opposite set, with which they must articulate and keep in occlusion.

This physiologic study is illustrated by numerous colored plates.

NEFF, Kansas City, Mo.

Pathology, Bacteriology and Biochemistry

THE EFFECT OF VAGOTOMY ON GASTRIC EMPTYING TIME. WALTER J. MEEK and RAYMOND C. HERRIN, Am. J. Physiol. **109**:221 (Aug.) 1934.

Thoracic vagotomy in the dog lengthens the final emptying time of the stomach. All evidence points to the vagus as a nerve necessary for the existence of normal gastric tonus and indicates that emptying depends in some way on the degree of this tonus.

NOURSE, Cleveland.

A CONVENIENT METHOD FOR DETERMINING SERUM AND BILE PHOSPHATASE ACTIVITY. EARL J. KING and A. RILEY ARMSTRONG, Canad. M. A. J. **31**:376 (Oct.) 1934.

A new method is described for estimating serum phosphatase activity in which the enzyme is allowed to act on phenyl phosphate and the liberated phenol is determined. The method is adaptable for use with bile. The time required for duplicate analysis of a serum is about one hour. The accuracy of the method is considered to be as great as or greater than that of previously described methods. The unit by this method is almost the same numerically as that of Jenner and Kay.

MOORE, Omaha.

THE DEVELOPMENT OF HYPERSENSITIVENESS IN MAN: I. FOLLOWING INTRADERMAL INJECTION OF ANTIGEN. FRANK A. SIMON and FRANCIS M. RACKEMANN, J. Allergy **5**:439 (July) 1934.

A group of atopic and nonatopic persons were given repeated intracutaneous injections of guinea-pig serum of different dilutions. The results would indicate that sensitiveness can be produced, as indicated by the reaction obtained by subsequent injection of serum.

The artificial sensitiveness was produced more rapidly and more regularly with the stronger dilutions and to the same extent and with the same ease in nonatopic persons. Antibodies capable of transferring the sensitiveness locally to the skin of a normal recipient may be demonstrated when the degree of sensitiveness, as measured by the skin test, is large but not otherwise."

HOYER, Cincinnati.

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was found to be the most valuable index of the severity of the disease in a given animal. Other factors which may influence the course and outcome of the disease are discussed.

KNICKERBOCKER, Dallas, Texas.

EXPERIMENTAL TYPE III PNEUMOCOCCUS PNEUMONIA IN MONKEYS: II. TREATMENT WITH AN ENZYME WHICH DECOMPOSES THE SPECIFIC CAPSULAR POLYSACCHARIDE OF PNEUMOCOCCUS TYPE III. THOMAS FRANCIS JR., EDWARD E. TERRELL, RENÉ DUBOS and OSWALD T. AVERY, J. Exper. Med. **59**:641 (May) 1934.

Since it had been found possible regularly to produce experimental pneumonia in monkeys similar to lobar pneumonia in man, it was of interest to the authors to determine the effect of treatment with specific enzyme on the course and outcome of the disease. The authors report the results of enzyme treatment of experimental pneumonia due to type III pneumococcus in forty monkeys. All the animals were treated within the first three days after infection. In the entire series of forty monkeys in which enzyme therapy was employed the mortality rate was 20 per cent. No attempt was made to ascertain the minimal amount of enzyme required.

Many technical difficulties have been encountered in attempting to produce enzyme preparations of uniformly high therapeutic activity and purity. The different lots of enzyme have as a result been inconstant in both these respects.

The result of this study indicates that the specific enzyme of bacterial origin which has a capacity to decompose the specific capsular polysaccharide of type III pneumococcus, thus rendering the bacteria readily susceptible to phagocytosis by the cells of the animal body, even in its present state of purity, exerts a favorable therapeutic effect on the course and outcome of experimental pneumonia due to type III pneumococcus in monkeys.

Treatment was followed by cessation of spread of the pneumonic lesion, sterilization of the blood and early recovery, except in animals in which the severity of the disease was extreme. The limitations of the therapeutic action of the specific enzyme in the presence of marked depression of the cellular reaction in infected animals are again emphasized.

KNICKERBOCKER, Dallas, Texas.

OCCURRENCE AND PERSISTENCE OF TYPE-SPECIFIC AGGLUTININS AND PROTECTIVE ANTIBODIES IN THE SERUM OF RABBITS FOLLOWING THE INHALATION OF LIVING PNEUMOCOCCI (TYPES I AND II). ERNEST G. STILLMAN, J. Infect. Dis. **54**:339 (May-June) 1934.

Rabbits exposed repeatedly to a spray containing type I pneumococci developed agglutinins in the blood serum which remained for a short while and protective antibodies which persisted for a long time. Animals exposed to type II pneumococci only occasionally developed agglutinins and protective antibodies for a short time, while those exposed to type III pneumococci never had any demonstrable agglutinins or protective antibodies.

TOOMEY, Cleveland.

AN UNSUCCESSFUL ATTEMPT TO DEMONSTRATE FILTRABLE FORMS OF BACTERIA WITH K. MEDIUM. ORVILLE R. KELLEY, J. Infect. Dis. **54**:360 (May-June) 1934.

Kelley tried to demonstrate filtrable forms of bacteria, using Kendall's K medium, but was unsuccessful.

TOOMEY, Cleveland

IMMUNIZATION OF GUINEA-PIGS TO THE VIRUS OF EQUINE ENCEPHALOMYELITIS. BEATRICE F. HOWITT, J. Infect. Dis. **54**:368 (May-June) 1934.

Apparently there is no immunity to Borna disease in susceptible animals (the rabbit and guinea-pig) that have recovered from California equine encephalomyelitis. The reverse does not seem true, however, and in rabbits immune to

Borna disease there seems to be some protection against equine encephalomyelitis. Howitt is not certain about the latter point but believes that the two diseases are distinct entities.

Howitt tried to immunize guinea-pigs against the virus of equine encephalitis, using suspensions variously treated with formaldehyde, glycerite of phenol, phenol and chloroform, but with unsatisfactory result. She did show, however, that if the animals survived the injections they were found to be immune. Immune serum and virus combinations, as well as live virus, conferred immunity. The duration of this immunity may last six or seven months and has no relation to in vivo neutralization. Immunity may be transferred when both parents or the mother alone is immune.

TOOMEY, Cleveland.

ELIMINATION OF BRUCELLA ABORTUS WITH THE MILK OF "CARRIER" COWS. REDVERS THOMPSON, J. Infect. Dis. **55**:7 (July-Aug.) 1934.

Thompson has shown that Brucella abortus may be constantly eliminated with the milk of cows classified as healthy "carriers."

TOOMEY, Cleveland.

ACTIVE IMMUNIZATION AGAINST TETANUS INFECTION WITH TETANUS TOXOID. D. H. BERGEY, J. Infect. Dis. **55**:72 (July-Aug.) 1934.

Bergey has concluded that alum-precipitated tetanus toxoid is better than toxoid without alum and believes that active immunity against tetanus can be produced by its use.

TOOMEY, Cleveland.

DISSOCIATION OF STREPTOCOCCI OBTAINED FROM ACUTE RHEUMATIC FEVER. KATHARINE M. HOWELL and ELEANOR P. BURTON, J. Infect. Dis. **55**:79 (July-Aug.) 1934.

Four strains of streptococci isolated from patients with acute rheumatic fever by Howell and Burton remained stable, smooth and virulent for eight months and did not become dissociated even under the most unfavorable circumstances, though there were elements of dissociation as suggested by pleomorphism and occasional S-R colonies.

TOOMEY, Cleveland.

ANTERIOR PITUITARY HORMONE AND OTHER PREPARATIONS INFLUENCING GONADAL ACTIVITY. F. E. CHIDESTER, M. J. & Rec. **139**:641 (June 20) 1934.

It is evident that the sex hormone extracted from iodine-rich substances could furnish a stimulus to the gonads that is identical with that induced by iodides. Not only animal sources of the sex hormone, but the plants and minerals yielding it, are known to be sources of iodine. Some preparations rich in chlorine might act as a halogen displacer of stored iodine also.

The other type of sex hormone, highly unsaturated (desaturated), which is so potent could be used in medicine because of its production of hyperactivity of glands such as the thyroid. That the unsaturated sterols and hydrocarbons are concerned in normal action of the vitamins and hormones has been known for some time. And evidence is now accumulating to show that the carcinogenic activity of certain estrogenic substances may be due to such an unsaturated condition.

WILLIAMSON, New Orleans.

THE GROWTH OF PERIOSTEUM IN LONG BONES. W. TURNER WARWICK and PHILIP WILES, Brit. J. Surg. **22**:169 (July) 1934.

Rabbits were used experimentally to determine the behavior of the periosteum on the growth of long bones. It was thought that an understanding of this might help to explain the sliding of muscle insertion and perhaps throw some light on the question of the relation of periosteum to bone limitation and modeling. The

experimental work is described in detail. The authors obtained results which caused them to arrive at the following conclusions:

Periosteal growth does not occur as in the underlying bone by increments from the epiphyseal lines, but by interstitial growth throughout its length; also, this interstitial growth is reasonably regular.

The process of ligament and muscle sliding during normal growth of long bones, and possibly also the limiting of growth and modeling of the bones, are related to the interstitial growth of periosteum. SUMMERFELDT, Toronto, Canada.

NEUROLYTIC PROPERTIES OF CEREBROSPINAL FLUID. R. GRECO, Ann. Inst. Pasteur **51**:265, 1933.

Nerve substance is destroyed in vitro by cerebrospinal fluid within forty hours. This action, which is probably enzymic, does not take place after warming to from 60 to 70 C. or in the presence of chloroform but is unaffected by thymol or pilocarpine. KUGELMASS, New York.

TYPES OF RESPIRATION IN CHILDREN OF BOTH SEXES. MILHAUD, Rev. franç. de puériculture **2**:117 (April) 1934.

The type of respiration differs in the two sexes before puberty, constituting a secondary sex characteristic. Formulas of coefficients of robustness for boys and for girls are derived from calculations of the vital capacity. CRANE, Chicago.

PHOSPHATEMIA AFTER INJECTION OF PHARMACODYNAMIC SUBSTANCES. P. MOLTENI and G. VANONCINI, Clin. pediat. **16**:681 (Aug.) 1934.

In a study of the effect of various substances on the inorganic phosphorus content of the blood in rabbits these investigators found that there was a constant increase in phosphorus after the administration of pilocarpine, a diminution after moderate doses of epinephrine and inconstant results after the administration of atropine (sometimes an increase, sometimes a decrease). They conclude, after due reservation because of the limitations of such research, that it is not possible to deny the influence of the vegetative nervous system on the phosphorus exchange, in the sense that vagal predominance is accompanied by a hyperphosphatemia and sympathetic predominance by hypophosphatemia. DOOLEY, New York.

EXPERIMENTAL STUDY ON HEMOGLYCOLYSIS. A. GENTILI, Riv. di clin. pediat. **32**:564 (May) 1934.

Gentili studied the glycolytic power of blood by comparing its sugar content before and after being kept at 37 C. for three hours. In thirty infants blood was drawn from the umbilical cord at birth. To 3 cc. of defibrinated blood 0.12 cc. of a buffer phosphate solution and 0.10 cc. of a 5 per cent solution of dextrose were added. The sugar was determined immediately in 1 cc. of the blood and in the remainder after it had been three hours in an oven at 37 C. The percentage of the sugar undergoing glycolysis was between 31 and 85, with an average of 46.

Comparisons of the glycolysis in maternal and fetal blood withdrawn at the same time showed greater glycolysis in each of seven cases in the fetal blood, the averages being: maternal blood, 26 per cent glycolysis; fetal blood, 47 per cent glycolysis. The percentage glycolysis in the blood of sixteen children from 2 months to 11 years of age averaged 26.5.

The addition of insulin to the blood in vitro did not increase the glycolysis. Injection of the insulin into the patient before withdrawal of blood resulted in increased glycolysis in both normal children and in a diabetic child.

HIGGINS, Boston.

THE CORN SMUT ENIGMA. F. PROUBASTA, Paidoterapia **13**:115 (June) 1934.

After centuries of laborious work the composition of smutted corn is at last known. Claviceps purpurea has two metabolisms: one corresponds to vegetable life and the other to animal life. By the first alkaloids are formed, and by the second, amines. Both act superficially on the uterus. The amines produce one uterine contraction for each dose, while the alkaloids provoke an intense and lasting contraction and therefore are capable of the phenomena of accumulations. In addition, the alkaloids exercise a paralyzing action on the sympathetic trunk, which is new in action, since no previously known drug does this.

HERRON, Spokane, Wash.

CONSUMPTION OF DEXTROSE IN HYPOPHYSECTOMIZED AND PANCREATECTOMIZED DOGS. ALFREDO BIASOTTI, Rev. Soc. argent. de biol. **10**:82 (May) 1934.

In previous works Biasotti demonstrated the attenuated character of diabetes in hypophysectomized dogs. The dogs survived longer; the loss of weight was slow; in general the blood sugar level was but little elevated over the normal level; the glycosuria was low and disappeared with starvation, and the dextrose-nitrogen ratio was consistently lower than the normal. Biasotti presents the conclusions drawn from experimental work on four dogs that were studied before and after pancreatectomy, and then before and after an additional hypophysectomy. He concludes that after pancreatectomy and hypophysectomy the respiratory quotient was elevated following the administration of dextrose. This increase was not noticed in the dogs after pancreatectomy alone. For this reason these hypophysectomized and pancreatectomized dogs frequently were able to burn a certain amount of dextrose without the use of insulin. A part of the sugar administered was retained and utilized, even in those dogs which did not have an increased combustion in the first hours following its administration. These dogs showed a greater tolerance to carbonic acid and carbon dioxide than the pancreatectomized dogs, and the blood sugar level was lower, with a slower rise and a more rapid fall of the blood sugar curve produced by the injection of dextrose.

HERRON, Spokane, Wash.

LACTIC ACID OF THE BLOOD IN HYPOPHYSECTOMIZED DOGS. A. D. MARENZI, Rev. Soc. argent. de biol. **10**:121 (June) 1934.

Marenzi concludes that the lactic acid of the blood in normal and in hypophysectomized dogs is practically the same.

HERRON, Spokane, Wash.

THE DEXTROSE TOLERANCE OF HYPOPHYSECTOMIZED DOGS. A. BIASOTTI, Rev. Soc. argent. de biol. **10**:124 (June) 1934.

Biasotti concludes that the dextrose tolerance is diminished in dogs after a hypophysectomy. There are a rapid rise in the blood sugar above the normal level and a slower descent to the normal after the intravenous administration of 1 Gm. of dextrose per kilogram of body weight. When the dextrose was administered by mouth the difference between the dogs with absence of the hypophysis and the normal dogs was insignificant. The dogs with lesions of the tuber cinereum also had a lessened sugar tolerance.

HERRON, Spokane, Wash.

Nutrition

NUTRITION AS A FACTOR IN CHILD DEVELOPMENT BASED ON STUDIES OF CHILDREN COVERING THE ENTIRE PERIOD OF GROWTH. W. R. P. EMERSON, Arch. Pediat. **51**:343 (June) 1934.

This article is a review of well known facts concerning nutrition; it cannot be profitably abstracted.

WADDELL JR., University, Va.

CHRONIC INTESTINAL INDIGESTION. PHILIP S. POTTER, Arch. Pediat. **51**:363 (June) 1934.

This article is a review of the possible etiology, clinical picture and treatment of chronic intestinal indigestion; it presents no new ideas on this subject. The article also contains several reports of cases. WADDELL JR., University, Va.

SAUERKRAUT JUICE FOR THE ACIDIFICATION OF EVAPORATED MILK IN INFANT FEEDING. C. V. RICE, Arch. Pediat. **51**:390 (June) 1934.

Rice gives the results in the cases of seventy-five infants fed mixtures of whole milk or evaporated milk acidified with sauerkraut juice. It is believed that sauerkraut juice as a means of acidifying milk has the advantages of palatability, digestibility, economy and simplicity in preparation and in all probability is antirachitic and antiscorbutic in effect. WADDELL JR., University, Pa.

A STUDY OF THE RELATIVE ANTIRACHITIC VALUE OF COD LIVER OIL, VIOSTEROL AND IRRADIATED MILK. T. G. H. DRAKE, FREDERICK F. TISDALL and ALAN BROWN, Canad. M. A. J. **31**:347 (Oct.) 1934.

A study of the antirachitic value of cod liver oil, viosterol and irradiated vitamin D milk on 529 Toronto infants, largely of British and northern European descent, was made under home conditions over a period of five winter months. The age of the infants at the initial examination varied from 3 weeks to 8 months. One, 2 or 3 teaspoonfuls of cod liver oil was prescribed for 137 of the infants. Three showed moderate or marked rickets during the five months. Difficulty in administering the cod liver oil may have accounted for these three cases. One hundred, 200, 400 and 800 Steenbock vitamin D units were administered to 186 of the infants. None of the infants showed rickets. From 20 to 40 ounces (591.4 to 1,182.8 cc.) of irradiated vitamin D milk, containing 35 Steenbock vitamin units per 20 ounces was prescribed for 141 of the infants. None of these showed rickets.

MOORE, Omaha.

EVALUATION OF THE CAPILLARY RESISTANCE TEST IN THE DIAGNOSIS OF SUBCLINICAL SCURVY. D. GREENE, J. A. M. A. **103**:4 (July 7) 1934.

The integrity of the capillary wall is affected by several influences of a chemical, physical and nervous nature. Thus, there is a seasonal influence, and there is a variability between persons. Such findings constitute a serious limitation to the use of the capillary resistance test for the diagnosis of subclinical scurvy. Greene's studies indicate a considerable variability when the same children were tested at different times. A positive capillary fragility test was found in 21.7 per cent of a group of well nourished children of preschool age, in 9.2 per cent of well nourished school children receiving an abundant vitamin C supplement to their diet and in 12.5 per cent of malnourished school children with a small supply of vitamin C. It is concluded that the capillary resistance test does not necessarily denote an insufficient intake of vitamin C. BONAR, Salt Lake City.

CREATINURIA IN ADOLESCENT MALES. A. B. LIGHT and C. R. WARREN, J. A. M. A. **103**:410 (Aug. 11) 1934.

The oral administration of 25 mg. of ephedrine sulphate three or four times daily causes a temporary cessation of creatinuria among adolescent males. No explanation is presented for this phenomenon. The drug, however, exerts practically no influence on the twenty-four hour creatinine and urinary outputs.

BONAR, Salt Lake City.

BLOOD INORGANIC PHOSPHORUS IN ALLERGY. LATHAN A. CRANDALL and SAMUEL M. FEINBERG, J. Allergy **5**:515 (July) 1934.

The inorganic phosphorus of the blood serum of seventy-five allergic adults averaged 3.57 mg. per hundred cubic centimeters; that of the blood serum of sixteen allergic children averaged 4.28 mg. The serum of twenty-two nonallergic adults contained 3.42 mg. per hundred cubic centimeters, and those of five nonallergic children contained 3.9 mg. Crandall and Feinberg believe that anticoagulants interfere with the determination of phosphorus in plasma, so that lower values may be obtained.

HOYER, Cincinnati.

THE RELATION OF MICROÖRGANISMS TO CAROTENOIDS AND VITAMIN A: I. THE OCCURRENCE OF CAROTENE IN BACTERIA. MARY A. INGRAHAM and CARL A. BAUMANN, J. Bact. **28**:31 (July) 1934.

Although vitamin A has not yet been reported to occur in bacteria, the presence of the biologically active pigment carotene has been demonstrated in many organisms. The presence of carotene may be roughly predicted on the basis of the color of the organism. Organisms of an orange shade generally contain it. No anaerobes were found to synthesize this pigment. The amount of carotene produced by a given organism varies with the medium on which it is grown. The content per gram of cells increases with age to a definite maximum, after which it decreases rapidly. The synthesis of carotene by bacteria, which was demonstrated by the authors on synthetic mediums, carries interesting biologic implications, since these micro-organisms do not contain chlorophyll.

STOESSER, Minneapolis.

NECESSARY VERSUS OPTIMAL INTAKE OF VITAMIN G (B_2). H. C. SHERMAN and L. N. ELLIS, J. Biol. Chem. **104**: 91, 1934.

The optimal intake of vitamin G (B_2) was determined by feeding rats mixtures of food equally rich in other known nutrients and with vitamin G values adjusted to four different levels. Enrichment by vitamin G of an already adequate diet resulted in superior vitality of the young animals, as well as extension of the period between the attainment of maturity and the onset of senility. There was increased growth in the young animals, as well as in their offspring. These findings show that the optimal intake is much above the amount which is demonstrated as strictly necessary.

MCBRYDE, Durham, N. C.

STUDIES OF THE ACID-BASE BALANCE OF THE BLOOD: I. A MICROTECHNIQUE FOR THE DETERMINATION OF THE ACID-BASE BALANCE OF THE BLOOD. NATHAN W. SHOCK and A. BAIRD HASTINGS, J. Biol. Chem. **104**:565, 1934.

A method is described for determining the acid-base balance of the blood on 0.1 cc. samples of blood from the finger. Using a specially designed pipet, the cell volume, carbon dioxide content and p_H of the blood are determined with accuracy.

MCBRYDE, Durham, N. C.

PASSAGE OF NATIVE PROTEINS THROUGH THE NORMAL GASTRO-ENTERIC WALL. BRET RATNER and H. L. GRUEHL, J. Clin. Investigation **13**:517 (July) 1934.

The anaphylaxis test was used as the biologic method of choice to determine whether native antigens enter the blood stream from the gastro-intestinal tract. Young and mature guinea-pigs were used, and precautions were taken to avoid creating abnormal conditions in the gastro-intestinal tract. It was shown that the animals could be sensitized by feeding milk and later shocked by intravenous injection, sensitized by intraperitoneal injection and shocked by feeding and both sensitized and shocked by feeding. The experiments were presented as conclusive

evidence that unsplit proteins pass the intact intestinal wall under normal conditions. An excellent review of the literature on this subject is given.

GUEST, Cincinnati.

EFFECT OF CARROT FEEDING ON THE SERUM PROTEIN CONCENTRATION OF THE RAT. ARTHUR L. BLOOMFIELD, J. Exper. Med. **59**:687 (June) 1934.

The concentration of serum protein falls in rats on an exclusive fresh carrot diet, but there was practically no lowering with the carrot powder diet; the addition of water and agar to the carrot powder serves to reproduce the effects which follow a diet of fresh carrots. Thus carrots contain no specific substance effective in lowering blood proteins and producing edema.

KUGELMASS, New York.

THE EARLY SIGNS OF VITAMIN A DEFICIENCY IN ALBINO RATS. FU-TANG CHU and ANNA MURPHY, J. Pediat. **5**:68 (July) 1934.

Albino rats were fed a diet deficient in vitamin A and were studied to find the earliest recognizable symptoms of vitamin A deficiency. The presence of cornified cells in vaginal scrapings and an increase in epithelial cells in the urine were found to occur before cessation of growth and ocular signs. There were no signs of impaired renal function during the course of the vitamin A deficiency.

LEMASTER, Evanston, Ill.

THERAPEUTIC USES OF MALTED MILK. JAMES A. TOBEY, M. Rec. **140**:18 (July 4) 1934.

Malted milk is made from barley malt, wheat flour and whole milk. The finished product is a powder and contains 69 per cent carbohydrates in the form of maltose, lactose and dextrin, and vitamins A, B and G, as well as fat, protein and minerals. It has an alkaline reaction. The therapeutic uses of malted milk are the same as those of cow's milk. It mixes readily with milk, adding to its caloric and nutritive values and improving the digestive properties. Malted milk is particularly efficient as a modifier for infants' feeding formulas, as a carrier for barium sulphate in roentgen work, as an adjunct in the dietary therapy of neuroses, insomnia and fevers and in all conditions in which a bland, easily digested diet is indicated. Physicians should always prescribe a standard product actually labeled as malted milk.

WILLIAMSON, New Orleans.

CLINICAL EXPERIENCE WITH VITAMIN D MILKS. J. M. LEWIS, New York State J. Med. **34**:685 (Aug. 1) 1934.

Vitamin D milks are very effective antirachitic agents and require fewer units to prevent or cure rickets than are necessary in the form of cod liver oil or viosterol.

AIKMAN, Rochester, N. Y.

STUDIES ON INFANTILE BERIBERI BASED ON 514 CASES. JOSÉ ALBERT, Philippine J. Sc. **45**:1 (Feb.) 1931.

This disease is responsible for 28 per cent of the mortality in Filipino babies under 1 year of age. Peculiarly, the mortality is greater in those breast fed than in the artificially fed, because the disease is due to the unbalanced diet of the nursing mothers.

There are three clinical forms: the aphonic; the pseudomeningitic, and the cardiac, which is the most important. The clinical symptoms come on abruptly in apparently perfectly normal babies. There are some vomiting, restlessness and crying for a few days. Then abruptly the baby begins to cry violently; there are cyanosis, dyspnea, pallor and enlargement of the heart, and death occurs in from twenty-four to forty-eight hours. The enlargement of the heart is associated with a weak pulse rate and accentuation of the second pulmonic sound.

Pathologically, there are hypertrophy and dilatation of the right side of the heart, with visceral congestion and anasarca, and in prolonged cases degeneration of the vagus nerve. Physiologically, the pathologic process is presumed to be due to the retention of water and consequent destructive swelling of the sarcoplasm. There is no degeneration of the myocardium.

The disease is usually observed between the second and third months of life in infants nourished by mothers suffering from incipient beriberi. It frequently happens that the mother having incipient beriberi becomes sick with clear manifestations of beriberi after the death of the infant. The disease is due to the unbalanced diet on which the mothers of these infants live—a little fish, a large quantity of rice and very few legumes. This diet is poor in protein, too rich in carbohydrates and deficient in calcium, sodium chloride and vitamins A and B.

The treatment consists in administering tikitiki extract (extract of rice polishings, Chamberlain and Vedder). Improvement is immediate, and Albert states that if treatment is begun in twelve hours it is always successful. The child is kept at the breast. It is interesting that tikitiki extract will revive an infant dying of heart failure, when digitalis, strophanthus, caffeine and other cardiac stimulants are ineffective.

SANFORD, Chicago.

THE VITAMIN E CONTENT OF CERTAIN DAIRY FEEDS. I. L. HATHAWAY and H. P. DAVIS, University of Nebraska, Agric. Exper. Stat., Research Bull. 73, August 1934.

This article consists of a report on the vitamin E content of various constituents of dairy feed. Female rats who were able to conceive but unable to reproduce when fed a diet deficient in vitamin E were tested with the various feeds. About 25 per cent of the bran, shorts, linseed oil meal, hominy feed, white corn, yellow corn, cottonseed meal, kafir or alfalfa furnished sufficient vitamin E to allow the rats to cast litters. On the other hand, 40 per cent of the corn gluten meal, the corn gluten feed or the beet pulp furnished very little vitamin E.

LEMASTER, Evanston, Ill.

VITAMIN A DEFICIENCY IN CHILDREN. HELEN M. M. MACKAY, Arch. Dis. Childhood **9**:133 (June) 1934.

Two groups of artificially fed babies were observed over a period of twenty-two months. The average period of attendance was approximately eight months. All were fed milk dried by a roller process, containing iron and ammonium citrate to which were added vitamin D, orange juice and sugar. Sixty children received in addition extra vitamin A; the other group (fifty-eight children), serving as controls, were dependent for vitamin A on that naturally present in their milk or other food (after 7 or 8 months of age).

The rate of growth in both groups was the same. The morbidity rates were similar in the two groups. Apparently the addition of vitamin A had no influence on general resistance to infection, whether to infections of the respiratory or the digestive tract or to specific fevers. The incidence of minor cutaneous infections, however, was approximately double in the control group what it was in the group receiving additional vitamin A.

From this study it would appear that diminished growth or diminished resistance to general infections is not among the first effects of slight vitamin A deficiency. However, the high incidence of infections of the skin in the control group is significant.

KELLY, Milwaukee.

BONE AND VEGETABLE BROTH. R. A. MCCANCE, W. SHELDON and E. M. WIDDOWSON, Arch. Dis. Childhood **9**:251 (Aug.) 1934.

On boiling veal bones with water or dilute acetic acid the loss of nitrogen is linear for at least the first seven hours. The loss of salts is complete in from one to two hours. On boiling vegetables with water the losses of nitrogen, sugar

and salts are very rapid at first and are almost complete in one hour. There is only a small loss of nitrogen when bones are soaked in water at room temperature, but the loss of salts is comparable with that at 100 C. Vegetables lose little of their constituents unless they are boiled. Figures are given for analyses of human and cow's milk and for broths made in different ways. Broths compare most unfavorably with milk in calorific value and salt content.

KELLY, Milwaukee.

THE TRANSMISSION OF VITAMIN A FROM PARENTS TO YOUNG IN MAMMALS: II. THE CAROTENE AND VITAMIN A CONTENTS OF COW'S COLOSTRUM. W. J. DANN, Biochem. J. **27**:1998, 1933.

The carotene content was measured by the yellow color of the unsaponified solution (in chloroform) as determined in a Lovibond tintometer. The vitamin A was determined by the blue color developed with antimony chloride. The vitamin A concentration in colostrum may be from ten to one hundred times greater than in later milk from the same cow. The carotene content of colostrum may be seventy times greater than in later milk. On the first day of life the calf receives supplies of vitamin A greater than the later milk could give in from twenty to fifty days.

KUGELMASS, New York.

A CUTANEOUS MANIFESTATION OF VITAMIN A DEFICIENCY. G. P. GOODWIN, Brit. M. J. **2**:113 (July 21) 1934.

Goodwin reviews the cases of vitamin A deficiency seen in China by Pillat, especially with reference to the cutaneous manifestations, which had a dry, scaly appearance with cystlike formation. Many of these patients in China showed xerophthalmia, night blindness and other conditions characteristic of vitamin A deficiency. Then follows a report of the case of an 11 year old boy with signs similar to those described by Pillat. Some of these manifestations were what would be called hornification by some observers. The diet of this boy had been very deficient in vitamin A. No treatment was given except improvement of the diet, which was balanced, and the administration of 4 drachms of cod liver oil a day. At the end of a week there was marked improvement, and by six weeks the skin looked almost normal, though there was still a little plugging in the sebaceous glands of the skin. On discharge the child was apparently normal in every respect.

ROYSTER, University, Va.

THE ANTISCORBUTIC VITAMIN. W. M. CAHILL, Bull. Soc. chim. biol. **15**:1462, 1933.

The juice of purple wine grapes has little or no antiscorbutic action. By a method similar to that used by Szent-Györgyi in the preparation of cevitamic acid from lemon juice a hexuronic acid was isolated from grape juice. It resembled cevitamic acid in many of its properties, but it had no antiscorbutic action. 5-keto-gluconic acid was prepared from dextrose by the action of Bacillus xylinus. It has no antiscorbutic action.

KUGELMASS, New York.

PATHOLOGIC PHYSIOLOGY OF MALNUTRITION IN INFANTS. L. GARAT, Nourrisson **22**:239 (July) 1934.

The clinical classification followed is that of Marfan: hypothrepsia of the first and second degree and athrepsia. The amount of panniculus adiposus determines the clinical diagnosis for any particular infant.

When these subjects are studied from the standpoint of the creatine and creatinine excreted in the urine it is found that in the milder cases of athrepsia there is no marked deviation from the normal figures, while in the more severe grades there are a slight lowering of the urinary creatinine and a marked diminu-

tion in the urinary creatine, pointing to a disturbance in the metabolism of the exogenous or alimentary nitrogen, probably owing to inadequate absorption.

Studies of the carbon-nitrogen ratio in the urine show that this is but slightly disturbed in the mild cases of athrepsia but almost double in the severe cases studied. This also gives evidence of marked disturbance in the nitrogen metabolism in the more profoundly affected patients.

Studies in basal metabolism show that in the mild cases of hypothrepsia the number of calories per kilogram of body weight per day run close to the normal figures of about 53. In the more severe cases the total calories per twenty-four hours are less than normal, but when expressed in calories per kilogram per day the basal rate is increased to 68 calories per kilogram per day. In the severe cases of denutrition in which there is reduction in the excretion of creatine, the calories per day are considerably diminished; the calories per kilogram per day are about normal (61.8), but the calories per square meter of body surface per day are reduced to 918 from a normal figure of 1,043. Special diets were fed in some cases to study the specific dynamic action of the proteins.

From his studies Garat concludes that two types of malnutrition in infants can be recognized: (1) a mild form of hypothrepsia characterized by a normal tissue metabolism and an ability to produce complete combustion of the food elements and (2) a severe grade of hypothrepsia or athrepsia characterized by some loss of intermediary metabolism with incomplete combustion of food elements.

McCLELLAND, Cleveland.

ALIMENTARY INTOLERANCE FOR EGG. LEON MEUNIER, Presse méd. **42**:1307 (Aug. 18) 1934.

A large amount of propaganda concerning intolerance for egg has brought about a veritable "egg phobia" in the minds of a great many persons. The food value of the egg is so great that it seems worth while to investigate the grounds for this prejudice. It has been claimed that egg produces hypercholesteremia. As the yolk of one egg contains only about 0.25 Gm. of cholesterol, it is hardly conceivable that even if all of it were metabolized the blood cholesterol would be appreciably affected. It is claimed, also, that the fat content of the egg-yolk is saponified with difficulty by persons with intestinal disturbances. The same persons, however, digest without difficulty four or five times the quantity of butter fat or cream.

A specific allergy to egg is another possibility. The breaking up of the heterogeneous albumin results in hemoclastic shock which may manifest itself as urticaria, nausea or gastro-intestinal pain. Meunier believes that since he found that the gastric acidity is greatly diminished by the ingestion of egg-yolk this might be utilized in overcoming the difficulty. He suggests that in persons evincing intolerance an acid solution be given with the egg to replace the abolished gastric acidity, or that some other animal protein be taken with it.

BIEKER, St. Petersburg, Fla.

USE OF MEAT IN INFANT FEEDING. A. IANCOU, Rev. franç. de pédiat. **10**:288, 1934.

Iancou reviews the practice of various pediatricians in regard to the use of meat preparations in infant feeding. Their content of vitamins, blood-forming elements and purine bases are factors which recommend their use in cases of malnutrition and even for the normal infant. He describes results from the use of a pudding made from flour, sugar, egg and liver. In instances in which milk was poorly tolerated an adequate diet could be constructed without any milk. Excellent results were obtained.

LESLIE, Evanston, Ill.

THE HORMONE SITUATION DURING EXPERIMENTAL RACHITIS. ALBERTO CABITTO, Pediatria **42**:927 (Aug.) 1934.

Cabitto reports observations which indicate that during experimental rickets there is an increased activity of the cortico-adrenal glands, as well as of the thymus gland. This functional activity was studied by means of enzyme reaction, and the changes were observed generally a few days after the institution of the rachitogenic diet. After the appearance of the primary signs of rickets the activity of the cortico-adrenals, of the thymus and of the posterior lobe of the hypophysis decreases, while the activity of the thyroid gland increases. The author believes that these conclusions suggest that rickets is accompanied by hypovagotonia determined by a decrease in the functional activity of the cortico-adrenals and the thymus gland.

SIGNORELLI, New Orleans.

CLINICAL COPROLOGY IN INFANCY. U. FIAMMINGHI, Prat. pediat. **12**:355 (Aug.) 1934.

This is a description of the usual stools of breast-fed and artificially fed babies and of the stools in various nutritional disturbances and in parasitic diseases. There is no information which may not be found in standard sources.

DOOLEY, New York.

STUDIES OF THE GASTRIC SECRETION OF INFANTS AND CHILDREN BY FRACTIONAL REMOVAL OF THE TEST MEAL. G. GIANNI, Riv. di clin. pediat. **32**:676 (June) 1934.

Gianni made analyses of the gastric secretions of twenty children ranging in age between 6 months and 12 years; the method of fractional removal of the contents of the stomach was used, samples being withdrawn at intervals of twenty-five minutes; the test meal was cow's milk diluted 1:3.

The gastric juice in the fasting child is of smaller quantity than in adults; it is of high digestive potency, containing in most cases free hydrochloric acid and the three gastric ferments.

Following the test meal, free hydrochloric acid was found in the contents of the stomachs of 71 per cent of the infants under 1 year of age and of but 37 per cent of the children between 1 and 2 years old. The pepsin and rennin in the gastric juice were highest when the free hydrochloric acid was highest. Gastrolipase, however, was not present in amounts proportional to the free hydrochloric acid.

The author thinks that in the 1 to 2 year old child protein digestion is more an intestinal function than in the older or younger child. HIGGINS, Boston.

PHOSPHATEMIA AND RICKETS. G. FRONTALI, Riv. di clin. pediat. **32**:897 (Aug.) 1934.

This paper is a lecture given before the "Biologische Gesellschaft" in Vienna and gives the author's views on the chemistry of rickets.

He draws the following conclusions:

1. A compound like hexose-monophosphoric acid or hexose-diphosphoric acid plays an important part in the cause and treatment of rickets.

2. This compound is split by actinic rays to increase the phosphate of the blood.

3. It constitutes a means by which one can measure, according to the amount of phosphorus freed, the action of direct and indirect actinic factors.

HIGGINS, Boston.

TREATMENT OF UNDERNUTRITION IN INFANTS BY SMALL DOSES OF INSULIN. A. VENUTI, Riv. di clin. pediat. **32**:924 (Aug.) 1934.

Venuti gave to ten undernourished infants one dose of insulin (from 1 to 6 units) daily for a period of two weeks up to three months. Following the injection

of the insulin from 20 to 35 Gm. of sugar was fed. In eight of the ten infants an average gain in weight of from 20 to 25 Gm. per day was noticed. Only one infant showed any symptoms of hypoglycemia. This child, a baby of 6 weeks, weighing about 2,500 Gm. and with probable hereditary syphilis, began to show the following symptoms one-half hour after the injection of 2 units of insulin: vomiting, pallor, a weak pulse rate, sweating and slight convulsive movements. An injection of dextrose stopped the symptoms, but further injections of insulin were not given.

HIGGINS, Boston.

POSSIBILITY OF DETERMINING BY A PRACTICAL METHOD THE AMOUNT OF PROTEIN IN HUMAN MILK. A. GALEOTTI-FLORI, Riv. di clin. pediat. **32**:972 (Aug.) 1934.

The author has devised a lactalbuminometer for determining the percentage of protein in mother's milk. The fat is first removed from the milk by centrifugating. One cubic centimeter of the fat-free milk and 1 cc. of the Folin and Denis sodium tungstate-orthophosphoric acid solution are mixed in the lactalbuminometer, an instrument similar to an Esbach albuminometer. After forty-eight hours the amount of protein can be read on a scale, as in determining albumin in urine. The method was checked by the Kjeldahl apparatus.

From an analysis of three hundred samples of human milk, the author found the protein to vary from 4.25 to 17.75 parts per thousand and to average 9.16 parts per thousand.

HIGGINS, Boston.

NUTRITIONAL UPSETS FROM INSUFFICIENT FEEDING. P. BUXO IZAGUIRRE, An. de pediat. **1**:356 (June) 1934.

There are two types of malnutrition. In one there is an insufficient quantity of food, and in the other a deficiency in quality. The author reviews the caloric requirements of normal infants and describes the symptoms and treatment of forms of nutritional disorders due to the following: underfeeding and diets deficient in water, in carbohydrates, in proteins, in fats, in salts and in vitamins.

HERRON, Spokane, Wash.

TREATMENT OF ATHREPSIA. JOSÉ M. ESTÉVEZ, Arch. de med. inf. **3**:688 (June) 1934.

Any kind of milk is of value to the patient if used in the initial stages of athrepsia. The addition of vitamins A, B, C and D by mouth or intracutaneously stimulates the assimilating capacity of the athreptic cells for the digested food, thus speeding up the recovery.

SANFORD, Chicago.

THE PROBLEM OF INFANT FEEDING. RUDOLF FISCHL, Paidoterapia **13**:211 (July) 1934.

At least during the early months of life the breast should be used, if possible. The breast milk contains antibodies and antitoxins which add to the defensive mechanism of the child. The colostrum is poor in fats and is easily digested. The small amount of breast milk obtained during the first week or two of life may produce a disturbance of the water metabolism. This is combated by the use of Karlsbad water in amounts of 100 cc. daily. The composition of breast milk is exactly adopted to the slow growth of the infant and its gastro-intestinal apparatus. It possesses important bactericidal properties and important ferments which assist in the subsequent digestion of the milk. There is no better galactagog than the child's own sucking. Fischl prefers the three hour interval between breast feedings.

After the third month the greater need for salts and vitamins is satisfied by the addition of purées and fruit juices to the diet. In premature infants small

injections of Leers' serum is advisable. Weaning is begun at the fifth or sixth month unless there is a predisposition to exudative diathesis, in which case it is postponed. Artificial feeding is more harmful the younger the infant. The Czerny-Kleinschmidt method of feeding is preferred. This author does not care for the feeding of buttermilk because of its low fat content and dislikes the use of flours. The contamination by bacteria is not as important as has been thought. The manufacture of dried milk is a step forward. Underfeeding as well as overfeeding must be borne in mind. The classification by Finkelstein of the disorders of infants caused by feeding is accepted as the best classification. There is an extensive description of the two groups, dyspepsia and decomposition. The diseases of the breast-fed infant run their course rapidly, while in the artificially fed infant they are much more serious. The author is definitely in favor of breast milk over other forms of feeding. HERRON, Spokane, Wash.

PROPHYLAXIS OF RICKETS IN THE PREMATURE AND CONGENITALLY DEBILITATED INFANT. A. MUNOYERRO PRETEL, Paidoterapia **13**:369 (Aug.) 1934.

The author gives an excellent up-to-date summary of the general physical, physiologic and chemical changes that occur in premature and congenitally debilitated infants. He suggests the prevention of premature births by better obstetric care, which in turn would prevent pediatricians from having to care for so many premature infants. To prevent rickets in these children measures must be taken at once or during the first week or two of life, without waiting the usual two months or so. He suggests that ultraviolet radiation be used regularly and believes viosterol to be less effective. He also gives a 10 per cent solution of tribasic calcium phosphate in cod liver oil as a prophylactic measure.

HERRON, Spokane, Wash.

SHALL WE USE NATURAL OR SYNTHETIC VITAMIN D? RAMOS PEREIRA, Pediatria, Rio de Janeiro **1**:210 (Sept.) 1934.

Pereira lists many of the undesirable results from the use of irradiated products reported in the literature and pleads for conservatism in their general use.

SANFORD, Chicago.

RÔLE OF THE VITAMINS IN NUTRITION. VICENTE BAPTISTA, Pediatria, Rio de Janeiro **1**:245 (July) 1934.

The author discusses the function of the various vitamins and appends a chart of their source, symptoms of their lack and the treatment of avitaminoses.

SANFORD, Chicago.

METABOLIC DISTURBANCES IN DIARRHEA OF INFANCY. JOSEPH CSAPÓ, Arch. f. Kinderh. **102**:165, 1934.

The metabolic changes caused by diarrhea in infancy are reviewed and discussed. There are many references to the studies of American investigators in this field. The most important effects of severe diarrhea include dehydration from loss of water, loss of basic minerals in the stools, loss of chloride ions in vomiting, decrease in digestive enzymes and secretions, effect of bacterial toxins and impairment of renal excretion. The author states that little is known of the intermediary metabolism of carbohydrates, proteins and fats in diarrheal diseases.

LEMASTER, Evanston, Ill.

PRESENT POSITION OF KNOWLEDGE OF VITAMINS. CHRISTIAN BOMSKOV, Arch. f. Kinderh. **102**:171, 1934.

The present conception of the nature and function of vitamins is discussed. Bomskov emphasizes the special need of growing organisms for vitamins. Follow-

ing classification of the vitamins there is a fairly complete summary of the modern knowledge of vitamin A, its chemistry, the physiology of its action, the symptoms and pathology of vitamin A deficiency and biologic tests.

LEMASTER, Evanston, Ill.

CHLORIDE CONTENT OF CAPILLARY AND VENOUS WHOLE BLOOD AND SERUM IN INFANCY. G. TÖRÖK and L. NEUFELD, Arch. f. Kinderh. **102**:217, 1934.

The chloride content of the blood serum of twenty-six normal infants under 4 months old was found to vary between 303 and 414 mg. per hundred cubic centimeters. In twenty-four sick infants (excluding those with vomiting and diarrhea) the serum chloride content varied between 297 and 424 mg. The chlorides ranged from 168 to 328 mg. in the capillary whole blood of the twenty-six well infants and from 167 to 304 mg. in the venous whole blood. In the sick infants the chlorides in the capillary whole blood lay between 204 and 320 mg. and in venous whole blood between 204 and 300 mg. The authors believe that their results may be accepted as standard for small infants and that a rather wide variation in the chloride content, such as they found, must be recognized as normal in infancy.

LEMASTER, Evanston, Ill.

PRESENT POSITION OF KNOWLEDGE OF VITAMINS. CHRISTIAN BOMSKOV, Arch. f. Kinderh. **102**:226, 1934.

The modern knowledge of vitamins B, C and D is summarized and briefly discussed from the clinical point of view. This is the second article of a series designed to acquaint the practicing physician with the latest information on vitamins.

LEMASTER, Evanston, Ill.

PARENTERAL ADMINISTRATION OF VITAMIN C IN THE TREATMENT OF SCURVY. E. E. BAUKE, München. med. Wchnschr. **81**:1240 (Aug. 10) 1934.

A sporadic case of severe scurvy with ulcerative gingivitis, anemia, suffusions, constant fever and psychic disturbances was dramatically improved by the daily intravenous administration of 100 mg. of l-cevitamic acid. The temperature was normal after the second day of the treatment, and the hemoglobin content rose rapidly.

BRAHDY, Mount Vernon, N. Y.

INCREASED SECRETION OF MILK INDUCED BY ANTITHYROID PROTECTIVE SUBSTANCE. H. KÜSTNER, München. med. Wchnschr. **81**:1261 (Aug. 17) 1934.

The only satisfactory methods for increasing lactation are massage and emptying of the breasts. Küstner found that the secretion of milk of mothers who for some reason were not to nurse their infants could be diminished rapidly by the administration of thyroxin. If an antagonistic action to the hormone of the thyroid gland could be produced artificially, the secretion of breast milk might be enhanced. Küstner gave alternate patients tablet preparations of the antithyroid hormone from the posterior lobe of the pituitary gland. The tablets were taken from the first day post partum without untoward effects. The secretion of milk in the treated mothers was greater and appeared sooner than in the untreated mothers. A few failures occurred in women who had small breasts or who had a family history of difficult lactation.

BRAHDY, Mount Vernon, N. Y.

HISTOLOGIC CHANGES INDUCED BY OVERDOSAGE OF VITAMIN A. G. DOMAGK and P. VON DOBENECK, Virchows Arch. f. path. Anat. **290**:385, 1933.

In rats that received daily by mouth 100,000 units of vitamin A concentrate, the Kupffer cells of the liver, the pulp cells of the spleen and the capillary endothelium of the kidney and lung contained fat. This change is ascribed to increased

fat resorption brought about by the vitamin. The squamous epithelium of the proventriculus became hyperplastic, its cells appeared immature, and hornification disappeared. The changes described occurred irrespective of the oil used as the solvent for the vitamin concentrate. The oils alone, sesame, peanut and paraffin oils, had no such effects.

SCHULTZ, Evanston, Ill. [ARCH. PATH.]

FATE OF ABSORBED FAT IN THE ORGANISM. HEINRICH SCHUR, ARTHUR LOW and ANTON KREMA, Wien. Arch. f. inn. Med. **25**:197 (Aug.) 1934.

In starving mice the introduction of a single meal of oil or fat can cause such an increase of the fat depot in the entire organism that it provides an experimental medium by which the influence of certain substances on the fat metabolism, particularly insulin, can be studied. Following the ingestion of fat, the lipoid content of the entire animal, including that of the liver and the connective tissue, rises parallel with the fat content. The carbohydrate content of the liver often diminishes after liberal feeding of fat, while that of the connective tissue regularly rises.

SCHLUTZ, Chicago.

EFFECT OF INSULIN ON TEMPORARY DEPOSIT OF ABSORBED CARBOHYDRATE AND FAT IN THE ORGANISM. HEINRICH SCHUR, ARTHUR LOW and ANTON KREMA, Wien. Arch. f. inn. Med. **25**:203 (Aug.) 1934.

The ingestion of carbohydrate definitely and directly increases the fat content of the experimental animal. Insulin seemed to enhance this action. The addition of fat has a similar effect. Small doses of insulin aided such a deposition in the tissues. The intake of carbohydrate increases the carbohydrate content of the entire organism, especially the liver. The simultaneous administration of insulin depresses this increase in the liver, as well as in the entire organism. The intake of fat diminishes the carbohydrate content of the liver and increases it in the connective tissue. Insulin aids such action and seems to have an indispensable function in the assimilation of fat and carbohydrate. The ingestion of fat and carbohydrate stimulates the secretion of insulin.

SCHLUTZ, Chicago.

PRESENT NUTRITIONAL CONDITION OF THE YOUTH IN LARGE CITIES. T. FÜRST, Ztschr. f. Gesundhführ. **1**:315, 1934.

Because of the increased burden which large-sized families have had to endure during the depression, the nutritional state of children has been impaired. The effects can still be seen in children who are about to leave school and enter an occupation. It is, therefore, necessary to give special consideration to such children who come from large families. The development of social service agencies in larger industrial plants has lead to definite improvement in the apprentices in such places. In smaller plants the conditions are still bad, and it would appear as though some legislation extending over the entire field of apprentices were necessary.

REICHLE, Cleveland.

INFLUENCE OF IRRADIATED ERGOSTEROL ON THE CIRCULATORY SYSTEM. L. DOXIADES and W. UHSE, Ztschr. f. Kinderh. **55**:137, 1933.

Doxiades and Uhse investigated the question of damage by the administration of viosterol. They found a definite increase of blood pressure in animals following the administration of viosterol. Electrocardiography showed changes in the final lead following the oral or intravenous administration of viosterol. The authors believe that the electrocardiographic results can be ascribed to the changes in the structure of the protoplasm of the heart muscles. The fact that the changes cannot be demonstrated pathologically does not speak against their presence.

LEVINSON, Chicago.

COLON AND PARACOLON BACILLI IN THE STOMACH AND STOOL IN NORMAL INFANTS AND IN THOSE SUFFERING FROM INTESTINAL DISTURBANCES. EUGEN DEAK, Ztschr. f. Kinderh. **55**:198, 1933.

Deak has studied the bacteria of the contents of the stomachs of twenty-eight healthy infants and of thirty-eight infants with various intestinal upsets such as mild dyspepsia, parenteral dyspepsia, severe dyspepsia and alimentary intoxication. He found that the content of the stomach of a healthy infant was either entirely sterile or contained streptococci, Staphylococcus albus, hay bacilli and Sarcina, which may be considered normal inhabitants of the stomach of the infant. In mild parenteral dyspepsia colon bacilli could always be demonstrated in the contents of the stomach. The stools in these cases contained the normal intestinal flora. In severe dyspeptic disturbances and in cases of alimentary intoxication both the stool and the stomach contained, in addition to colon bacilli, paracolon bacilli in various amounts. In some of these cases only paracolon bacilli could be demonstrated. When the infants improved the colon bacilli and paracolon bacilli in the stomach decreased in amount, but it was only after they disappeared entirely from the stomach that the stool became normal. Deak claims that whenever paracolon bacilli are found in the stool of a dyspeptic infant after the infant has improved there is always the possibility of a recurrence, even though there is normal digestion, with a normal stool. In infants who died with the clinical picture of alimentary intoxication the jejunum and large intestine always contained colon bacilli and paracolon bacilli in the same proportion found in the stomach and stool in the last days of the patient's life. Deak is not ready to state whether the paracolon bacillus is to be considered as a special form or as a mutation of the colon bacillus in diseases of the intestines. Nor is he ready to state whether the paracolon bacillus has a pathogenic significance or is only an indicator of some disturbance of the gastro-intestinal tract.

LEVINSON, Chicago.

DEMONSTRATION OF TOXIC SUBSTANCE IN SEVERE DYSPEPSIA OF INFANTS. K. HASSMANN and EUGEN DEAK, Ztschr. f. Kinderh. **55**:248, 1933.

Filtrates of the stools of infants suffering from severe dyspepsia were injected intracutaneously into guinea-pigs by Hassmann and Deak. They found positive reactions with filtrates of stools obtained during the disease and negative reactions with filtrates of stools obtained after the dyspepsia had subsided. The toxic substance was not destroyed by boiling for five minutes. The filtrates of the stools of children with acute dyspepsia were alkaline, and after the infants improved the filtrates lost their alkalinity. The authors are of the opinion that the endogenous variations of the virulence of the colon group play an important rôle in the etiology of intestinal disturbances.

LEVINSON, Chicago.

ALLEGED TOXIC ACTION OF COD LIVER OIL AND CONCENTRATES OF VITAMIN A. M. E. BELL, E. GREGORY and J. C. DRUMMOND, Ztschr. f. Vitaminforsch. **2**:161, 1933.

A disturbance of growth of rats occurs when their diet containing 2 per cent of cod liver oil is supplemented with 15 per cent of cod liver oil and sufficient vitamin B complex. This disturbance may be alleviated by increasing the amount of the vitamin B complex. The apparent toxic effect was not caused by vitamin A itself, by nitrogenous bases in fish liver oils, by an oxidation product of cod liver oil or by an overdosage of vitamin D and could not be produced by the ingestion of large amounts of provitamin A (carotene). No evidence that rats "overdosed" with cod liver oil failed to assimilate it or that it affected the normal reaction of the gastric and intestinal contents was obtained.

KUGELMASS, New York.

ANTISCORBUTIC PROPERTY OF ADRENAL CORTEX. R. DEOTTO, Ztschr. f. Vitaminforsch. **2**:182, 1933.

Aqueous extracts of adrenal cortex (acidulated with citric acid in a dilution of 1:3) have an antiscorbutic power, while similar extracts from liver have no such property, and neither has epinephrine.

KUGELMASS, New York.

IS THERE A VITAMIN A HYPERVITAMINOSIS? G. ROSSI, Ztschr. f. Vitaminforsch. **2**:194, 1933.

Rabbits and guinea-pigs showed no unfavorable effects with large doses of vitamin A, but in white rats this treatment resulted in diarrhea. Large doses of vitamin A, together with an overdose of vitamin D, retarded the growth of rabbits.

KUGELMASS, New York.

Prenatal Conditions

DIAPHRAGMATIC HERNIA IN A CHILD. J. P. NALBANT, Am. J. Roentgenol. **28**:635 (Nov.) 1932.

A colored child of 6 was examined six months previously and found normal on roentgenologic examination. There was no history of trauma, infectious disease or other definite complaint. Clinically there was impaired resonance in the apex of the left lung at the axilla and in the base, but no râles, friction rub or fluid. Roentgenologically, following the ingestion of barium sulphate, the stomach and intestines were seen to occupy the left side of the chest, with a shifting of the mediastinum and heart to the right. The possible causes of such a noncongenital herniation are: (1) dissection of the diaphragmatic muscle from its posterior attachment, with a peeling away of the parietal pleura by the herniated structures; (2) rupture of the diaphragm near the posterior attachment and (3) a weak, undeveloped diaphragmatic muscle which might stretch sufficiently to allow the ascent of the abdominal viscera, but which would continue to keep separate the abdominal and thoracic viscera. The third possibility is the most likely. Because of the lack of symptoms no diagnosis could have been made without the roentgen examination.

STULIK, Chicago.

DIAPHRAGMATIC HERNIA WITH SEVERE ANEMIA. MAX WEITZEN, Am. J. Roentgenol. **28**:808 (Dec.) 1932.

Up to 1923 only forty-seven cases of diaphragmatic hernia were diagnosed during life. Harrington reported three with severe anemia in a series of thirty patients operated on. The number of cases in which this condition is diagnosed is rapidly increasing. Weitzen reports two cases in adults, one of whom had persistent gastric bleeding from the herniated stomach. The other patient had also intermittent bleeding from the incarcerated cardiac portion of the stomach. In the differential roentgenographic diagnosis one must consider (1) eventration of the diaphragm, (2) hour-glass stomach and (3) esophageal diverticula. Demonstration of the diaphragmatic arches is most important. Clinically the substernal pain and pressure must be differentiated from those in angina pectoris and sclerosis of the coronary artery.

STULIK, Chicago.

CONGENITAL HEART BLOCK. W. M. YATER, W. G. LEAMAN and V. H. CORNELL, J. A. M. A. **102**:1660 (May 19) 1934.

Congenital heart block is not as rare as is ordinarily supposed. Six cases have been studied at necropsy, and in four serial sections of the conduction system have been made. In the case reported the interauricular septum and the membranous portion of the interventricular septum were almost completely lacking. There was nearly complete separation of the auricles and ventricles by the central fibrous body where the bundle normally bridges the auriculoventricular groove.

The bundle of His was well formed but was not connected with the auriculoventricular node in this region. Certain criteria are used for the diagnosis: (1) the auriculoventricular dissociation must be proved by graphic methods in a young subject, (2) the bradycardia must be noted at an early age and (3) a history of any infection which might cause heart block after birth must be absent.

BONAR, Salt Lake City.

CONGENITAL STENOSIS OF THE LARYNX. R. W. WILKINSON, J. A. M. A. **102**:1756 (May 26) 1934.

True congenital stenosis of the larynx is limited to atresia, bands or webs within the glottis, involving the vocal cords, ventricular bands or arytenoids, and is permanent unless relieved surgically. This condition should not be confused with the relatively unimportant congenital stridor resulting from abnormal flaccidity of the epiglottis. The author reports a case of the atresic type in which there was atresia of the free borders of the vocal cords anteriorly, reducing the glottis to one-half its normal size. The bands were separated, and since then there have been no cyanotic attacks, and the child, aged 7, can speak, huskily but audibly. The embryonic fusion theory seems to be the most generally accepted and most tenable explanation. Embryologically there is a period of fusion of the structures of the glottis, apparently to prevent the passage of amniotic fluid down the respiratory tract. Later, about the eleventh week, there is a period of dissolution, with separation of the arytenoid folds, followed by parting of the superior and inferior folds to form the ventricular bands and the vocal cords proper. When stenosis occurs it is due to incomplete separation of these processes. The diagnosis is made by direct laryngoscopy, and the treatment depends entirely on the severity of the stenosis.

BONAR, Salt Lake City.

THE KLIPPEL-FEIL SYNDROME (CONGENITAL WEBBED NECK). H. S. MITCHELL, Arch. Dis. Childhood **9**:213 (Aug.) 1934.

Six cases of congenital webbed neck are described. Two anatomic specimens are recorded. In each of these the normal number of intervertebral foramina were present, although one could not identify all the individual bodies of the corresponding vertebrae. As the vertebral body and vertebral arches come from the same sclerotome, it would appear that the condition is the result not of a diminution in the number of the vertebrae but rather of an irregular fusion and conglomeration of the bodies. There is usually a large exposed portion of the spinal cord and its membranes in the upper cervical region. This is a false spina bifida, as the spine is not bifid, since the arches meet in an abnormally low position.

KELLY, Milwaukee.

CONGENITAL ABSENCE OF THE ABDOMINAL MUSCLES. L. G. HOUSDEN, Arch. Dis. Childhood **9**:219 (Aug.) 1934.

A case of congenital absence of the abdominal muscles is described in detail. The observations at autopsy are given. Various views on the cause of the condition are described, and it is shown in a discussion that the absence of the abdominal muscles is due to the atrophy of previously formed muscles by pressure from an enormously dilated bladder and ureters, such pressure being probably increased by secondary ascites. The cause of the dilatation and hypertrophy of the bladder is considered to be an organic obstruction in the urethra. KELLY, Milwaukee.

COMPLETE CONGENITAL DIAPHRAGMATIC HERNIA IN AN ADULT. JOHN F. HACKWOOD, Brit. M. J. **1**:1030 (June 9) 1934.

A girl, aged 20, who had hitherto been healthy and well, so far as any symptoms were concerned, was operated on because of severe pain in the region of

the left shoulder. At operation the hernia was discovered, with most of the abdominal contents in the thoracic cavity. The patient died the seventh day after the operation.

ROYSTER, University, Va.

CONGENITAL DEFORMITIES OF THE MOUTH. DENIS BROWNE, Practitioner **132**:658 (June) 1934.

Browne gives a good description of the congenital deformity caused by the failure of junction between the fetal parts that should form the upper wall of the mouth. The five distinct regions involved are: the regions of the lip, the floor of the nostril, the alveolar ridge, the hard palate and the soft palate. A careful presentation of the surgical method of repair of the cleft of the upper lip is given.

Browne stresses the three dangers to healing: (1) Tension. This he suggests may be avoided by the proper use of Logan's bow. (2) Nasal mucus. This irritating substance may be prevented from reaching the surgical wound by good nursing care through the application of small loosely rolled pledgets of cotton-wool to the nostrils, which are changed as soon as they become soaked. (3) Sepsis of the skin. This may be entirely avoided by the use of an ointment of 1 part flavine to 1,000 parts liquid petrolatum, applied to the wound in small quantity daily.

The surgical technic used in the treatment of the other four congenital deformities of the upper wall of the mouth is also presented.

SAPPINGTON, San Francisco.

CONGENITAL MALFORMATION OF THE NECK (KLIPPEL-FEIL'S DISEASE OR WEB-NECK). ERIC PRITCHARD, Proc. Roy. Soc. Med. **27**:1007 (June) 1934.

The case reported was that of a girl of 3 months. A photograph of the head of the child and a roentgenogram of the upper part of the spine accompany the report.

WILLIAMSON, New Orleans.

CONGENITAL STENOSIS OF THE HEPATIC DUCT. J. V. BRAITHWAITE, Proc. Roy. Soc. Med. **27**:1008 (June) 1934.

The case of a boy of 1 year is reported. Six days after admission to the hospital, pneumonia developed, and the patient died. The report of the postmortem examination, with microscopic pictures of sections of liver, is also given.

WILLIAMSON, New Orleans.

FETAL MONSTROSITY WITH TWO FACES. GUÉRIN-VALMALE and PLASSE, Bull. Soc. d'obst. et de gynéc. **23**:362 (May) 1934.

A woman 23 years old at about five and a half months of pregnancy was delivered of a male fetus weighing about 1,000 Gm. It appeared normal below the neck except for lumbosacral spina bifida. The head, which was large, presented two complete faces, one looking obliquely right and the other obliquely left. The spinal canal was divided into two parts in the upper thoracic and cervical regions, and there appeared to be two atlas bones. A photograph of the fetus and the roentgenogram are shown.

GLASER, Rochester, N. Y.

ARACHNODACTYLIA AND SUBLUXATION OF THE LENS: OBSERVATIONS IN ONE FAMILY. H. VILLARD, H. VIALLEFONT and J. TEMPLE, Bull. Soc. d'opht. de Paris, July 1934, p. 384.

The family described consisted of the father, the mother and five children. The father and the first, the second and the fourth child had congenital ectopia lentis, the lenses being dislocated above and laterally. The first and the second child had arachnodactylia. The lenses of the children were normal, but those of

the father showed peripheral opacities under the anterior cortex. The authors were unable to trace the father's family tree, as he had entirely separated himself from all the other members. There were no traceable stigmas in the mother's antecedents. General examination of every member of the family failed to reveal any outstanding finding. Pictures and drawings accompany the article.

MAYER, Chicago. [ARCH. OPHTH.]

PHOSPHATEMIA IN THE PREMATURE INFANT. JUAN P. GARRAHAN and CARLOS M. PINTOS, Arch. argent. de pediat. **5**:432 (Aug.) 1934.

The authors determined the inorganic phosphorus in the blood serum of twenty premature infants and found in general an elevated level of blood phosphates in the premature infant over that observed in full-term infants. The method of Fiske-Subbarow was used.

SCHLUTZ, Chicago.

RETROPHARYNGEAL DIVERTICULUM IN AN INFANT. JOSÉ QUEIROZ, Arch. de pediat., Rio de Janeiro **6**:815 (June) 1934.

This condition was discovered at the autopsy of a 1 year old dystrophic infant who died of diffuse bronchopneumonia. The diverticulum had produced a large cavity with the prevertebral aponeurosis so that food taken entered and filled it and thus caused asphyxial symptoms.

SANFORD, Chicago.

HETEROTOPIC INTESTINAL MUCOSA IN THE STOMACH. F. CLAR, Beitr. z. klin. Chir. **160**:145, 1934.

In fetuses up to the seventh month the stomach may contain either single or grouped intestinal crypts. Intestinal mucosa was found in the stomach of a full-term infant; also in six of ten stomachs resected for pyloric ulcer. Islands of intestinal mucosa are most frequent in the pyloric region and the lesser curvature. They may become the seat of inflammatory and ulcerative lesions.

EDITOR'S ABSTRACT [ARCH. PATH.]

BIPARTITION OF THE FIRST CUNEIFORM BONE IN INFANCY. E. FRIEDL, Röntgenpraxis **6**:193 (March) 1934.

Pfitzner first observed this anomaly in 1896, noting a dorsal first cuneiform and a plantar first cuneiform separated by a horizontal interline and each having a center of ossification. It is rarely seen in adults, but sometimes there appears a mere line showing where the two parts have united. In a roentgenogram of the dorsoplantar region taken obliquely the dorsal cuneiform bone inclines inward, while the plantar bone inclines outward, concealing the second cuneiform bone. In children the condition is easily recognized, because these positions are reversed. The dorsal cuneiform is the smaller of the two.

VINTON, Brooklyn.

A CASE OF TRUE HERMAPHRODITISM. K. STOJALOWSKI and J. DEBSKI, Virchows Arch. f. path. Anat. **290**:358, 1933.

The authors tabulate nine previously reported examples of true hermaphroditism. In all but one of these the gonad was a combined ovary and testis. In their case, in which operation was performed following the diagnosis of incarcerated right inguinal hernia, there were a hypoplastic uterus and a right ovariotestis, with graaffian follicles and corpora haemorrhagica, and seminal tubules with stages of spermatogenesis but no spermatozoa. In the rudimentary scrotum was a small left testis from which by puncture living spermatozoa were obtained. This patient menstruated regularly from a hypospadiac urethra. The breasts and escutcheon were of the female type, but the body build was male. The sexual feeling was male.

Nocturnal emissions had occurred from time to time, and the subject had had intercourse with women, with orgasm and ejaculation.

SCHULTZ, Evanston, Ill. [ARCH. PATH.]

THE AXIAL SKELETON IN ANENCEPHALY AND CRANIORACHISCHISIS. B. DEPPE, Virchows Arch. f. path. Anat. **293**:153, 1934.

Study of a series of fetuses presenting varying grades of anencephaly and craniorachischisis led Deppe to conclude that maldevelopment of the central nervous system is the primary anatomic factor, to which the failure of union of the bones of the cranium and vertebral column is secondary. Ribs and vertebral bodies are formed in normal numbers but are often fused. The characteristic distortions of the spinal column are the result of mechanical factors, such as pressure and muscular traction, to which the open vertebral column is less resistant than the closed one.

SCHULTZ, Evanston, Ill. [ARCH. PATH.]

STUDIES ON THE ORIGIN AND BIOLOGICALLY INHERITED FACTORS IN CONGENITAL MALFORMATIONS. ERNST GÜNTER ABRAHAM, Ztschr. f. Geburtsh. u. Gynäk. **109**:187 (Aug.) 1934.

Abraham presents the case histories of four infants with congenital malformations. The first has hydrocephalus, spina bifida and malformation of the ribs; the second, hydrocephalus, spina bifida and clubfoot; the third, hydrocephalus, and the fourth, a large umbilical hernia.

Complete family histories are included. In all cases except that of the third infant transmissible defects are present in either the maternal or the paternal line or both. Although Abraham does not deny that congenital malformations may be caused by factors operating after fertilization of the ovum, he believes the greatest cause to be the transmitted tendencies present in the genes of the ovum or sperm cell. In general, the state of potential abnormality is inherited and is not a specific defect.

ADAIR and POTTER, Chicago.

A HISTOLOGIC STUDY OF THE CARTILAGE OF THE LOWER END OF THE HUMAN FEMUR IN EVERY FETAL STAGE. E. TERADA, Jap. J. Obst. & Gynec. **17**:186 (June) 1934.

Terada presents a series of observations of the histologic development of cartilage in the human femur, describing the changes as they occur in each fetal month.

In the second fetal month, the chondrifying stage, those cells which were destined to form cartilage revealed distinctive changes. The cells of the superficial stroma were fibroblastic, whereas the deeper cells varied in size and shape. In the third fetal month each type of cells became larger and showed evidences of mitosis and proliferation. In the fourth fetal month rapid enlargement of the cartilage of the bone end was noted, and the nutritive apparatus, consisting of the nutritive blood vessels and cartilaginous medulla, began to take form. In the fifth, sixth, seventh and eighth fetal months the growth of the cartilage of the bone ends was most intense, and the cartilage showed evidence of increased proliferation and mitosis. By the eighth month small depositions of granules of lime were observed, which were to form by the ninth month the ossifying nuclei. In the ninth and tenth fetal months the growth and proliferation of the cartilaginous cells and parenchyma were lessened, but the growth of the ossifying mechanism in the bone ends progressed. Similarly, the nutritive apparatus, which had shown increased growth, began to lessen markedly in growth activity to the time when ossification began to progress in these cartilaginous bone ends.

ADAIR and BENENSOHN, Chicago.

DYSTROPHIA BREVICOLLIS CONGENITA. HERMAN NIELSEN, Hospitalstid. **77**:409 (April 10) 1934.

A girl of 12 years was a dwarf, diminutive in height rather than across the shoulders. This shortness of stature was seen to be due to truncation of the lower extremities, while the body, arms and head were in normal proportion; also to the neck, which a single glance showed to be foreshortened, so that the head set too close to her body. This shortening of the neck limited the movements of the head both laterally and forward and backward. Furthermore the neck was very broad, appearing as though the trapezius muscle lapped over on both sides. Her hair was profuse and coarse and fell in a heavy braid on each side. Abundant lanugo was in evidence, especially along the spinal column. On the other hand, the axillae were devoid of hair, and there was little on the pubis. A slight asymmetry appeared in the face, because the right half was somewhat larger than the left; and there were perceptible exophthalmos of the right eye and slight ptosis of the left; the eyebrows were normal. Her facial expression was lively and her intelligence normal. The facial asymmetry caused her eyes to stand too far apart. A remarkable peculiarity was that the ears were situated very low down: when she was looked at squarely in front they appeared to be on a level with her mouth; when they were seen from one side this was not so conspicuous. The posterior cerebral fossa was unusually deep, and the cranial and frontal planes were wholly globular.

VINTON, Brooklyn.

A PECULIAR CASE OF CONGENITAL MULTIPLE TUMORS IN THE LIVER IN A CHILD FOUR MONTHS OLD. J. W. SCHMELLING, Nederl. tijdschr. v. geneesk. **78**:3566 (Aug. 4) 1934.

Necropsy performed on a boy of 4 months with several congenital anomalies—bilateral hydrocele, hypospadia glandis penis and bilateral syndactylia of the second and third toes—showed that the large tumor in the abdomen was an enlarged liver (as had been previously demonstrated) containing many large tumors. Microscopically, these consisted of: irregular liver cords, large spaces lined with endothelium and filled with blood, bile ducts, poorly developed blood vessels and embryonal connective tissue. These tumors belong to the hamartoblastomas as described in 1907 by Eugen Albrecht.

VAN CREVELD, Amsterdam, The Netherlands.

Diseases of the New-Born

PNEUMONIA IN NEWBORN AND STILLBORN INFANTS. MARGARET WARWICK, Am. J. M. Sc. **187**:253 (Feb.) 1934.

Pneumonia in the new-born is a definite entity and usually begins in utero or during birth. Most of the victims have physical handicaps; consequently the pneumonia may be a result of lowered resistance, although the exciting cause is uncertain. Present evidence seems to favor either contamination of the amniotic fluid by bacteria or an irritating amniotic fluid, particularly when it contains large amounts of bile and cornified epithelial cells. The comparative reasons favoring each theory are outlined, the majority of which are seemingly in favor of the latter etiology.

HENSKE, Omaha.

THE PREVENTION OF INITIAL LOSS OF WEIGHT IN THE NEWBORN BY THE USE OF A HYDRATING SOLUTION. L. J. HALPERN, J. Pediat. **5**:40 (July) 1934.

As originally suggested by Kugelmass, an isotonic solution consisting of 6 per cent gelatin, 3 per cent dextrose and 0.5 per cent sodium chloride was fed every two hours to seventy-five new-born infants. A similar number of new-born infants fed by various usual methods by the bottle or at the breast or both every three to four hours served as controls. The infants who received the hydrating solution

showed an initial loss of weight of 1.14 per cent less than the controls and regained their weight at birth from 1.3 to 1.5 days sooner than the controls. The administration of the fluid for the first two days of life yielded the best results.

LEMASTER, Evanston, Ill.

THE TREATMENT OF ERYTHROBLASTOSIS OF THE NEWBORN. DOUGLAS P. ARNOLD and RICHARD A. DOWNEY, New York State J. Med. **34**:591 (July 1) 1934.

Arnold and Downey prefer the term hyperplastic-hemolytic anemias of the new-born. They urge early detection of icterus gravis and advise repeated estimations of the hemoglobin (several daily, if necessary) to differentiate the condition from severe physiologic icterus. In many cases the placenta is enlarged and edematous. The condition is best treated by properly given repeated transfusions by cutting down on the internal saphenous vein. Several cases are reported briefly.

AIKMAN, Rochester, N. Y.

ANEMIA OF THE NEWBORN. ROGER H. DENNETT and LESLIE O. ASHTON, New York State J. Med. **34**:595 (July 1) 1934.

A case of primary anemia of the new-born is reported in which recovery followed treatment by transfusions. About thirty-six instances have been found since Ecklin reported the first case in 1919. The two outstanding features of this anemia are the lack of etiologic factors and the tendency to get well.

AIKMAN, Rochester, N. Y.

TREATMENT OF EPIDEMIC PEMPHIGUS OF THE NEW-BORN BY APPLICATION OF SILVER NITRATE AND ULTRAVIOLET RADIATION (METHOD OF HULDSCHINSKY). V. CATHALA and J. MEYER, Bull. Soc. franç. de dermat. et syph. **41**:673 (April) 1934.

Huldschinsky has shown that if silver nitrate after its local application is reduced by exposure to a source of light rich in ultraviolet rays its antiseptic action is enhanced. Cathala and Meyer recommend the method in the treatment of bullous impetigo of the new-born. A 3 to 5 per cent solution is painted over the ruptured bullae, and its reduction by ultraviolet irradiation is rapid, no erythema being necessary. It was found that many infants needed only two or three such treatments, though some required as many as six, given over a period of eight days. No infant was hurt by the treatment. Two points were impressive, namely, (1) the swiftness of the epidermic regeneration over large excoriated surfaces and (2) the rapidity with which the black spots of silver nitrate disappeared from around the bullae—they generally subsided in three days, while it takes twelve days or more for such stains to disappear from healthy adult skin. In the discussion Jausion states that the method was originally intended for rebellious eczema and is particularly applicable to ulcers resulting from varicose veins.

GANDY, Houston, Texas [ARCH. DERMAT. & SYPH.]

POSTNATAL CARE. FLORENCIO ESCARDÓ, Semana méd. **1**:1030 (April 5) 1934.

The author discusses the following topics: the technic of ligation of the cord, the loss of weight of the new-born during the first week of life, the treatment of conjunctivitis in the new-born and the treatment of pernicious vomiting of the new-born by the use of maternal blood. Nothing new is added.

HERRON, Spokane, Wash.

MORPHINISM OF THE NEW-BORN. E. MENNINGER-LERCHENTHAL, Monatschr. f. Kinderh. **60**: 182, 1934.

In a review of the literature the author reminds that morphinism in the new-born is not uncommon. When a new-born infant whose mother is a morphine

addict shows diarrhea, collapse and convulsions soon after birth, morphinism must be considered. The treatment consists of 1 drop of laudanum every half hour until the symptoms are relieved. If the mother has been taking more than 10 grains (0.65 Gm.) a day, the dosage for the infant should be increased.

GERSTLEY, Chicago.

WEIGHT OF THE THYMUS IN NEW-BORN INFANTS. P. R. RUSSKOFF, Virchows Arch. f. path. Anat. **293**:113, 1934.

The weight of the thymus, absolute and relative to body weight, was determined in 841 infants who came to necropsy in the pathologic institute of the University of Bern, Switzerland, during the years 1908 to 1932 inclusive. Premature and full-term infants who died within the first month of life were included, as were also stillborn infants. The material was divided into five groups according to body weights. In general, the weight of the thymus was slightly higher in male infants than in female infants of the same group. In a group of infants who were at least 50 cm. long and who lived not longer than twenty-four hours, the average weight of the thymus was 11.8 Gm. in males and 12.5 Gm. in females, and in the two sexes it was 12.1 Gm. The relation of thymus weight to body weight was 1:271.8 (0.37 per cent). The thymus was heavier in anencephalic infants than in normal infants of the same weight. In the later months of fetal life the growth of the thymus parallels that of the body. The weights of the thymus and thyroid gland did not parallel each other. The average weight of the thymus in the goiter district of Bern did not exceed that of other regions.

SCHULTZ, Evanston, Ill. [ARCH. PATH.]

FOUR CASES OF UNUSUAL ICTERUS IN NEW-BORN INFANTS. A. VAN WESTRIENEN, Maandschr. v. kindergeneesk. **3**:466 (Aug.) 1934.

Four cases of unusual icterus are described. The first case was one of severe familial jaundice in the new-born. In this case treatment of the mother with large amounts of liver did not prevent the disease in the baby. The second case was one of common but severe icterus neonatorum in a family in which already four infants had died of severe familial jaundice. The third case was one of severe anemia in a new-born infant with a large number of nucleated red cells, perhaps belonging to the group of so-called congenital anemia. The fourth case was probably a case of infectious cholangeitis.

VAN CREVELD, Amsterdam, The Netherlands.

HYDROPS UNIVERSALIS FOETUS ET PLACENTAE. D. VAN VUGT, Nederl. tijdschr. v. geneesk. **78**:2339 (May 26) 1934.

Five cases of this condition are described with a discussion of the symptomatology and pathogenesis. In the author's opinion the cause may be a (hormonal?) disturbance of the reticulo-endothelial system of the fetus, causing destruction of blood, followed by regeneration, and disturbance of the water metabolism. Analogous changes are found in the mother, which disappear a short time after the child has been born.

VAN CREVELD, Amsterdam, The Netherlands.

Acute Infections

THE RELATION BETWEEN VITAMIN A METABOLISM AND SUSCEPTIBILITY TO DIPHTHERIA TOXIN. CALVIN C. TORRANCE, Am. J. Hyg. **18**:375 (Sept.) 1933.

The survival time of guinea-pigs after an injection of diphtheria toxin was not increased by feeding increased amounts of vitamin A. A high degree of correlation was found between the vitamin A stored in the livers and the survival time, but no such relation existed between these stores and the amount of vitamin A fed except with animals raised on a diet deficient in vitamin A.

KUGELMASS, New York.

BACILLARY DYSENTERY IN CALIFORNIA. ALFRED C. REED, Am. J. M. Sc. **187**:819 (June) 1934.

This disease is considered to be widespread in California on an endemic basis from which institutional and local epidemics arise. Bacillary dysentery is an example of a so-called tropical disease. When the incubation period exceeds one to seven days, the infection is usually one that has been lying dormant in the intestine without symptoms until the clinical disease is aroused by some intercurrent agent. A résumé of the pathologic picture, diagnosis, means of spread, incidence and treatment are given. The severity is influenced largely by the type of bacilli. The Flexner type is milder and more common in California and the Shiga type more severe and less frequent.

HENSKE, Omaha.

ALTERATIONS IN THE MINERAL CONSTITUENTS OF ANTERIOR HORN CELLS IN EXPERIMENTAL POLIOMYELITIS. W. E. PATTON, Am. J. Path. **10**:615, 1934.

The principal type of destruction of nerve cells in poliomyelitis involves three stages: (1) edema, with acute swelling of the cell and diminution of its inorganic content; (2) granulation, with hypermineralization, and (3) acidophilic necrosis, with diminution of the mineral constituents.

FROM THE AUTHOR'S SUMMARY [ARCH. PATH.]

EVALUATION OF DIPHTHERIA TOXOID PREPARATIONS AND METHODS OF IMMUNIZATION. JOHN D. MONROE and V. K. VOLK, Am. J. Pub. Health **24**:342 (April) 1934.

Using one, two and three injections of New York City Health Department toxoid (8½ antigenic units per cubic centimeter) without alum and with 0.2 per cent alum added, Monroe and Volk found that the most practical and efficacious method was the injection of the alum-treated toxoid in two doses of 1 cc. each. This method produced immunity in 85.5 per cent of children with positive Schick reactions in two months and in 93.1 per cent in twelve months. Toxoid of from 7½ to 10 antigenic units was preferable to more concentrated toxoids. Toxoid with 0.28 per cent alum causes a slightly higher frequency of local reactions, and a moderate general reaction occurred in 74 per cent of cases.

McBRYDE, Durham, N. C.

VACCINE PREPARED FROM CHICKEN EMBRYO CULTURES FOR IMMUNIZATION AGAINST SMALLPOX. JULIA M. COFFEY, Am. J. Pub. Health **24**:473 (May) 1934.

Using the method described by Li and Rivers, cultivation of vaccine virus in a medium consisting of minced chicken embryo tissue suspended in Tyrode's solution, it was found that the virus gradually decreased in potency, but that the potency could be regained by passage through the testicles of rabbits. This vaccine can be stored at low temperatures for long periods without loss of potency, provided that air is excluded. In children vaccinated with the virus characteristic primary vaccinia developed, but the percentage of takes was lower than in children vaccinated with calf lymph.

McBRYDE, Durham, N. C.

SUBMAXILLARY MUMPS: CLINICAL REPORT OF FIVE CASES. S. LLOYD JOHNSON, Arch. Pediat. **51**:240 (April) 1934.

Five cases of submaxillary mumps are reported, which, with a number of other cases seen or known about but not reported, constitute what might be considered a mild endemic.

The incubation period appeared to be about from eighteen to twenty days, and the onset was sudden. In all the cases reported the patient was exposed to

epidemic parotitis, but none had ever had an attack of mumps previously. There was no regularity in the involvement of the submaxillary glands, either or both glands having been affected. One or both parotids were affected in half the cases. The sublingual gland was not affected in any of these cases. In three of the cases the condition began with an initial "cold," and the temperature was elevated to 103 F. during the height of the attack. The five cases were fairly mild, and the disease had run its course in one week; no complications developed in any case.

A brief review of the literature on such cases is given.

AUTHOR'S SUMMARY. (WADDELL JR., University, Va.).

DIPHTHERIA—DIAGNOSIS, THERAPY AND PROPHYLAXIS. THEODORE MELNICK, Arch. Pediat. **51**:431 (July) 1934.

This is a practical review of diphtheria from the standpoint of diagnosis, therapy and prophylaxis, which does not lend itself well to abstracting.

WADDELL JR., University, Va.

STUDIES OF THE NEWER STABILIZED SCHICK TOXINS. H. E. THELANDER, Arch. Pediat. **51**:454 (July) 1934.

The commercial preparations of Schick diluents have been perfected to a highly satisfactory degree.

Final readings of Schick reactions in adults should not be done earlier than the fourth day and preferably on the sixth or seventh day, allowing the early slight pseudoreaction to disappear. If pseudoreactions are severe and persistent, the blood should be tested for antitoxic content rather than subject the patient to repeated Schick tests. Many persons who give atypical reactions or pseudoreactions to Schick tests are immune.

Negative Schick reactions may be read without a control, but positive reactions cannot, for some pseudoreactions are persistent over several days and leave a stain not unlike the Schick test stain.

WADDELL JR., University, Va.

SOME ASPECTS OF VIRUS INFECTION WITH SPECIAL REFERENCE TO VIRUS DISEASES OF CHILDREN. J. CRAIGIE, Canad. M. A. J. **31**:347 (Oct.) 1934.

In this second Blackader Lecture Craigie gives an excellent review of the most recent views in regard to viruses.

In smallpox the virus seems to be identical with the Paschen bodies found in the vesicle fluid of smallpox and vaccinia. It is suggested that in cases in which there is a delay between contact with virulent smallpox and vaccination immune serum or blood be administered.

In chickenpox Aragao and, later, Paschen isolated elementary bodies similar to those of smallpox vesicles. There was no agglutination in antiserum from animals hyperimmunized against vaccinia. Amies found a cross-agglutination between zoster and chickenpox elementary bodies and zoster and chickenpox convalescent serums.

The measles organism is an outstanding example of a virus which can be completely controlled by immune serum therapy.

The virus nature of mumps has been definitely indicated by the work of Gordon and of Wollstein and recently established beyond question by Johnson and Goodpasture.

Poliomyelitis is discussed in detail, and Farber's view concerning the strict confinement of poliomyelitis virus to the central nervous system in man is accepted with some reservations. The value of immune serum in the treatment of poliomyelitis is still unproved. Craigie believes that the immune serum deserves a further trial under circumstances whereby the observations can be completely controlled and should be given only intravenously.

MOORE, Omaha.

IMMUNIZATION AGAINST THE CONTAGIOUS DISEASES OF CHILDHOOD: DIPHTHERIA, SCARLET FEVER, WHOOPING COUGH AND MEASLES. LAWSON WILKINS, Internat. Clin. **2**:266 (June) 1934.

In the past fifteen years the value of active immunization against diphtheria has become generally recognized. The use of diphtheria toxoid has now largely replaced that of toxin-antitoxin. Its advantages are higher efficiency in immunization, absence of sensitization to animal serum, greater stability and the fact that few doses are required. The use of a concentrated toxoid precipitated by alum apparently produces immunity following a single injection. Because of its simplicity the single dose method will probably become the method of choice. Löwenstein's ointment is less effective than other methods and would have its use only when there is objection to injections by needle.

The Schick test should be performed after immunization. Even when the reaction has become negative there is always the possibility that infection may occasionally occur. Immunization reduces the risks of infection to a minimum, but it is not an absolute guarantee.

Epidemiological studies have shown that the immunization of even a high proportion of school children (from 50 to 70 per cent) has failed to affect the morbidity and mortality from diphtheria in the community. However, when 30 per cent or more of the children under 5 years of age have been immunized in addition to the older children, diphtheria is reduced to negligible proportions in the entire population.

The lack of positive assurance that the conferred immunity is a lasting one, the realization that the Dick test is a fairly accurate but not positive guarantee of immunity and the rather frequent unpleasant reactions, together with the mild type of scarlet fever prevalent in this country, make one hesitate to recommend active immunization of all susceptible children at present.

Immunization with large doses of raw toxin, which is now used, has proved effective in controlling epidemics and in protecting persons in institutions where they are especially liable to exposure. Under these circumstances active immunization should be recommended. However, present-day knowledge concerning the toxin and the immunization is still far from complete.

MILLER, South Bend, Ind.

DIPHTHERIA TOXOID. J. L. WHITE and E. A. SCHLAGETER, J. A. M. A. **102**:915 (March 24) 1934.

Studies were made of the relative immunizing value of a given diphtheria toxoid with and without the addition of alum and of the optimum dosage from the standpoint of amount, the number of doses and the interval between doses. The results previously obtained with commercial toxin-antitoxin in Chicago were reviewed. The authors found that the alum toxoid furnished by Dr. Park of the New York Department of Health was somewhat more effective in producing immunity than the same lots of toxoid with no alum. In this series 96.1 per cent of 295 children were immunized with the alum toxoid in two months and 100 per cent of 254 children in six months, as compared with 94.6 per cent of 263 children and 95.9 per cent of 213 children in six months with the alum omitted. The studies showed that there was no decided advantage in using an interval of three weeks between doses, as compared with an interval of one week. Three doses of 0.5 cc. of the Park alum toxoid at weekly intervals were less effective than two doses of 1 cc. at intervals of a week. The series in which one dose of both reagents was used was decidedly less effective in producing the desired immunity. For instance, a single dose of the Park alum toxoid produced immunity in but 50.8 per cent in two months and 73.2 per cent in six months, while for the toxoid without alum the figures were 49.2 and 82 per cent, respectively. These lots of toxoid with and without alum, when given in the proper dosage, proved to be more effective than three doses of commercial toxin-antitoxin formerly used in Chicago.

BONAR, Salt Lake City.

DURATION OF IMMUNITY FOLLOWING VACCINATION AGAINST SMALLPOX. W. P. DEARING and M. J. ROSENAU, J. A. M. A. **102**:1998 (June 16) 1934.

In the experience of Dearing and Rosenau, all persons properly vaccinated exhibit a "take." Failure to take indicates faulty technic of some sort or an inactive virus. The reaction following the initial vaccination is called the primary take. If the patient has been vaccinated before, the modified reaction is classified as immediate or accelerated, indicating the retention of some immunity. Occasionally when the subject loses all his immunity to cowpox a primary take may follow revaccination. Studies made on 557 medical students who had been vaccinated revealed the welcome fact that immunity conferred by a single vaccination usually lasts longer than from seven to ten years and that it extends for twenty years or more in most persons. Revaccination reenforces protection and is usually mild. Such findings do not alter the procedure of revaccinating when exposure has occurred or there is danger of exposure.

BONAR, Salt Lake City.

CONVALESCENT SCARLET FEVER SERUM AND COMMERCIAL ANTITOXIN. P. S. RHOADS and B. J. GASUL, J. A. M. A. **102**:2005 (June 16) 1934.

In the experience of Rhoads and Gasul the ordinary commercial preparations of scarlet fever antitoxin have always given complete protection against scarlet fever in susceptible persons when administered before the onset of the disease. Using the method for titrating commercial antitoxins, it was found that twelve lots of pooled convalescent serum contained so few neutralizing units per cubic centimeter as compared with the requirements for commercial antitoxin that at least thirty times as much convalescent serum would be required. Since convalescent serum is being used so extensively it seems pertinent to suggest that there is a quantitative element in scarlet fever therapy that cannot be overlooked. It is apparent that insufficient amounts of convalescent serum are being given at present and that such doses are not comparable with the effects of commercial antitoxins.

BONAR, Salt Lake City.

THE USE OF DIPHTHERIA TOXOID IN IMMUNIZATION OF MEDICAL STUDENTS AND NURSES. A. E. KELLER and S. HARRIS JR., J. A. M. A. **102**:2163 (June 30) 1934.

Diphtheria in medical students and nurses is a significant problem in spite of the lower susceptibility rate in this age group. It is possible to immunize students and nurses against diphtheria with diphtheria toxoid without producing undesirable reactions. Those who might have a severe reaction can be detected by testing intradermally with a dose of dilute toxoid. Inoculations of dilute toxoid should be given those reacting in this manner. The observations of the authors emphasize the desirability of replacing toxin-antitoxin with diphtheria toxoid as an immunizing agent.

BONAR, Salt Lake City.

MASSIVE SKIN GANGRENE COMPLICATING CHICKENPOX. T. M. WATSON, J. A. M. A. **102**:2179 (June 30) 1934.

Gangrene of the skin developed in a boy, aged 6, shortly after onset of chickenpox. The area of gangrene, 15 cm. wide, extended from just below the axilla to the crest of the ileum on the right side. The patient was profoundly toxic, and the gangrene, which was preceded by intracutaneous hemorrhage, continued to spread. Repeated transfusions and the administration of parenteral fluid were of decided value in the treatment of the condition. The patient was discharged in good condition after two months.

BONAR, Salt Lake City.

THE ARTHUS PHENOMENON. F. E. ROSS, J. A. M. A. **103**:563 (Aug. 25) 1934.

A boy, 4½ years of age, who had been immunized for diphtheria with toxin-antitoxin a year previously was given a prophylactic dose of tetanus antitoxin for an injury to the scalp and three days later a therapeutic injection of scarlet fever antitoxin because of a rash and fever simulating scarlet fever. The site of injection became erythematous and indurated, and an area of fulminating necrosis appeared, spreading rapidly to involve the skin and subcutaneous tissues of the entire thigh, hip and abdomen. The patient died as a result of sepsis. This case, which was considered one of the Arthus phenomenon, stresses the importance of using toxoid, which contains no serum, in diphtheria immunization and emphasizes the necessity for extreme caution in the administration of any type of serum to a patient showing symptoms that might be manifestations of anaphylaxis.

BONAR, Salt Lake City.

THE RELATION OF RHEUMATIC FEVER TO POSTSCARLATINAL ARTHRITIS AND POSTSCARLATINAL HEART DISEASE: A FAMILIAL STUDY. JOHN R. PAUL, R. SALINGER and B. ZUGER, J. Clin. Investigation **13**:503 (May) 1934.

In families of patients who had sustained an attack of postscarlatinal nonsuppurative arthritis or carditis a high incidence of various manifestations of rheumatic fever was found. The findings are presented to support a view that these scarlatinal sequelae are not necessarily specific complications of scarlet fever, but are more easily explainable as manifestations of rheumatic fever activated by an infection due to Streptococcus haemolyticus.

GUEST, Cincinnati.

PHYSIOLOGICAL DISTURBANCES DURING EXPERIMENTAL DIPHTHERITIC INTOXICATION: IV. BLOOD ELECTROLYTE AND HEMOGLOBIN CONCENTRATIONS. D. C. DARROW, H. YANNET and M. K. CARY, J. Clin. Investigation **13**:553 (July) 1934.

In the blood of rabbits given injections of diphtheria toxin the following changes were found: (1) a progressive increase in the hemoglobin concentration, (2) an approximately equal decrease of sodium and chloride in the serum, (3) decreased serum bicarbonate, (4) a marked increase in the serum inorganic phosphate, which paralleled the severity of the intoxication.

GUEST, Cincinnati.

INACTIVATION OF POLIOMYELITIS VIRUS AND OF DIPHTHERIA TOXIN BY ENDOCRINE PRINCIPLES. C. W. JUNGEBLUT, K. MEYER and E. T. ENGLE, J. Immunol. **27**:43, 1934.

The virus of poliomyelitis was inactivated in vitro by certain biologic products of human and animal origin containing anterior pituitary-like principles and by the adrenal cortical and medullary hormones. Diphtheritic toxin was inactivated in vitro by preparations of the urine of pregnancy and by adrenal cortical hormone.

FROM THE AUTHORS' SUMMARY [ARCH. PATH.]

WHOLE BLOOD TRANSFUSIONS AS A TREATMENT FOR SEPTICEMIAS IN CHILDREN. H. R. ROEHM and H. B. BARKER, J. Michigan M. Soc. **33**:299 (June) 1934.

Roehm and Baker report from St. Joseph's Mercy Hospital at Pontiac, Mich., the treatment of six children with septicemia by the transfusion of whole unmodified blood.

In one case the condition was due to Staphylococcus albus, in three to nonhemolytic streptococcus and in one to an infection with nonhemolytic streptococcus and an unidentified diphtheroid organism. Two of the six patients had generalized peritonitis, demonstrated by abdominal paracentesis, with examination of fluid directly and by culture.

The authors believe that with an early diagnosis the injection of whole unmodified blood, repeated as indicated, is useful in this type of infection.

CAREY, Detroit.

DICK TESTS AND DICK TOXINS. THOMAS N. HORAN, J. Michigan M. Soc. **33**:301 (June) 1934.

Horan summarizes the results of five years' effort to prevent the invasion of scarlet fever into the Cranbrook School. This boarding-school with an average population of two hundred boys averaging 14.6 years of age has been free from scarlet fever for four and one-half years. The average immunity at the interval is 77 per cent. While reactions were encountered, they averaged but two thirds of a school day.

CAREY, Detroit.

TETANUS INFECTION TREATED WITH ANTITOXIN AND AVERTIN. F. A. HARRISON and H. L. HIGGINS, J. Missouri M. A. **31**:305 (Aug.) 1934.

Four cases of tetanus are reported from the children's wards of the Massachusetts General Hospital, one being of the cephalic type. In addition to the administration of tetanus antitoxin, avertin was given on two occasions in the first case, six times in the second, three times in the third and once in the fourth.

It is suggested that by the use of avertin the dose of antitoxin may be much diminished, which may be both economical and beneficial. The dose given was 80 mg. per kilogram of body weight; however, the authors' inclination is to give 100 mg. per kilogram in the future. Avertin was administered according to dosage tables and the technic advised by the manufacturer. The literature is quoted on reports of more than 300,000 cases in which avertin was administered by outstanding physicians. They seem to show that the damage to the liver and other organs is not great with proper dosage.

BERGER, Kansas City, Mo.

THE PRESENT STATUS OF SERUM THERAPY IN PEDIATRICS. JULIUS H. HESS, Nebraska M. J. **19**:288 (Aug.) 1934.

Antitoxins, antibacterial serums and their combinations and human convalescent serums are discussed.

Diphtheria antitoxin represents one of the greatest advances in applied immunology. Intramuscular injection is recommended for mild cases, intravenous and intramuscular injection for severe ones. Early treatment and adequate dosage are the guiding principles.

In the prophylactic treatment of tetanus the use of 1,500 units of serum injected promptly after the injury is accepted as the correct procedure. If operation is needed later, another injection should be given. If tetanus has developed, the convulsions should first be controlled with avertin given by enema; lumbar puncture should be avoided, if possible, and from 60,000 to 200,000 units of serum should be given intravenously in one dose. Careful nursing is necessary at all times to provide fluids, nourishment, change of position, sponges and baths, aid in prevention of the aspiration of mucus from the nasopharynx and the treatment of serum reactions. Blood transfusions may be necessary.

In erysipelas, the age, the severity and the distribution of the lesions affect the results. Very young infants show the least response. Convalescent serum (from 60 to 80 cc.) sometimes gives satisfactory results. Hess had gratifying results from repeated intramuscular injections of whole blood (from 20 to 40 cc.), especially in young infants.

The use of scarlet fever serum for prophylaxis is not recommended. In toxic cases occasionally the antitoxins are useful. Convalescent serum, which is now available in Chicago, has given some striking results. A dose of from 40 to 50 cc., which may be repeated, is advised. The author cites F. M. Mender as having treated four hundred and fifty contacts with 7.5 cc. of pooled serum;

the disease developed in 2.9 per cent, whereas 12.8 per cent of thirty-two control untreated contacts contracted the disease. Repeated transfusions of properly typed whole blood have produced gratifying results in toxic and even septic cases of scarlet fever.

In the treatment of meningitis, if the patient is seen early, antimeningococcic serum is given intravenously, especially if petechiae are present. Intraspinal injection of the serum is used, of course. In the treatment of pneumonia, rheumatism, dysentery and infections with pus organisms serum therapy still remains of limited value in children. While there have been unfavorable reports as to the value of convalescent serum in poliomyelitis, the results in four cases seen by the author recently again stimulated his interest. In measles, chickenpox, mumps and pertussis convalescent serum is of some value in prophylaxis, and in some cases there is modification of the disease if it has been contracted.

There is promise of further success in the development of serum therapy.

HAMILTON, Omaha.

THE VALUE OF COMMERCIAL ANTIBACTERIAL STREPTOCOCCUS SERA IN HEMOLYTIC STREPTOCOCCUS INFECTIONS. LE ROY D. FOTHERGILL and ROLF LIUM, New England J. Med. **211**:99 (July 19) 1934.

Prior to studying the commercial serums, observations were made on four patients with scarlet fever, using Ward's modification of Todd's technic. Blood was taken from each patient during the convalescent period (on the twenty-first, sixteenth, eighteenth and twenty-eighth day of the disease). The blood of the two patients without complications possessed essentially no bactericidal power. The blood of the two patients with complications possessed a not inconsiderable bactericidal power. One cubic centimeter of the blood of each of the latter two was able to kill approximately 20,000 organisms.

Observations were made on the bactericidal power of three different commercial antibacterial hemolytic streptococcic serums. These serums were purchased while fresh on the open market. Fifteen different strains of hemolytic streptococcus were used. Each of the fifteen organisms was tested with serum A and serum B. Eight strains were tested with serum C. Human blood (the authors') was used throughout this study. In each test blood alone was used as a control. This was done to be sure that there was no natural bactericidal power in the blood. Serum was used in final dilutions of 1 : 10, 1 : 100 and 1 : 500.

There was no killing of bacteria by serum A with any of the fifteen strains tested. With serum B, in two instances, with the 1 : 10 dilution of serum, there was a killing of the organism beyond a 10^{-4} dilution of the culture. Relatively, an enormous amount of serum was used compared with the number of bacteria killed and the amount of whole blood used. With serum C, in no instance was there evidence of any bactericidal power.

GENGENBACH, Denver.

CURRENT PREVALENCE OF COMMUNICABLE DISEASES IN THE UNITED STATES. Pub. Health Rep. **49**:783 (July 6) 1934.

For the period of May 20 to June 16 the number of cases of poliomyelitis in California rose to 801. Of these, 416 occurred in the city of Los Angeles, 270 in Los Angeles County (outside of the city of Los Angeles) and 36 in San Francisco. For the same period 110 cases were reported in other states, representing an increase of 48 per cent over the same period of 1933. This was confined to the western sections, as the New England states reported fewer cases, and the East South-Central group the same number as in 1933.

Measles and scarlet fever both show the usual seasonal decline. The incidence of diphtheria was the lowest on record for the previous six years. The average mortality rate was about the same as formerly, namely, 11 per thousand.

SANFORD, Chicago.

CURRENT PREVALENCE OF COMMUNICABLE DISEASES IN THE UNITED STATES, JUNE 17—JULY 14, 1934. Pub. Health Rep. **49**:905 (Aug. 3) 1934.

During the four weeks ending July 14 there were 1,309 cases of poliomyelitis reported in the United States, of which number 700 were in Los Angeles city and county and 410 in the remainder of California, with only 199 cases in the other states. An increase in typhoid fever was apparent in all sections of the country, but this fact is not especially significant, as the incidence usually increases sharply at this season of the year. The incidence of diphtheria, meningococcic meningitis and smallpox was definitely lower than that of the last few years. The number of cases of measles and scarlet fever declined from the preceding four week period, but was slightly higher than the reported number for the corresponding period of the last two years.

LEMASTER, Evanston, Ill.

SUMMARY OF CURRENT PREVALENCE OF COMMUNICABLE DISEASES IN THE UNITED STATES, JULY 15—AUGUST 11, 1934. Pub. Health Rep. **49**:1011 (Aug. 31) 1934.

For the period of July 15 to Aug. 11, 1934, there was a steady decline in cases of poliomyelitis for the state of California. There was a total of 466 cases for this period. Nearly all the Western States reported scattered cases, and in some states the number was running into epidemic proportions. A number of states east of the Mississippi River reported more than the usual expected number. There was some increase of typhoid fever in the drought area. In the west north-central area there were 408 cases of the period, as against 165 for the same period last year. Other contagious diseases showed the usual incidence. The average mortality was 10.5 per thousand, which is slightly in excess of former years.

SANFORD, Chicago.

SUMMARY OF CURRENT PREVALENCE OF COMMUNICABLE DISEASES IN THE UNITED STATES, AUGUST 12—SEPTEMBER 8, 1934. Pub. Health Rep. **49**:1129 (Sept. 28) 1934.

For the period of Aug. 12 to Sept. 8, 1934 poliomyelitis still continued above normal in the Western states. A résumé of the cases reported shows that the total number of cases for the seventeen week period was 4,816, which is only about one half of the total cases reported in 1931. This is, however, about 75 per cent above the figure for 1933 and 150 per cent above that for 1932. The number of cases of typhoid fever reported for the period was 3,335. This is the lowest number of cases for this period in the last six years. Other contagious diseases showed a normal incidence. The average mortality rate was 9.7 per thousand, which is average.

SANFORD, Chicago.

THE USE OF ADULT BLOOD IN WHOOPING COUGH. WALTER D. BROWN, Texas State J. Med. **30**:216 (July) 1934.

Brown points out that for some time convalescent serum and whole blood have been used either to prevent or to modify attacks of measles. The same idea applied to whooping cough is of recent development in the United States, though it was used by certain French workers as early as 1923. Brown observed from his series that the same rule applies as in measles; the result depends somewhat on the amount of blood given but in greater degree on the time when it is given.

If his results are confirmed, the author believes that adult whole blood or convalescent serum is an effective agent for early therapeusis, or, if given still earlier, for temporary passive immunity. In other words, one may expect results in whooping cough closely analogous to those from the use of this same measure in measles.

The author mentions the use of the vaccine which has been used by L. W. Sauer during the past five years for active immunity, to be used prophylactically, as toxoid is used in relation to diphtheria, and states that it is 100 per cent effective, provided that the children are not exposed to whooping cough under four months following vaccination.

KNICKERBOCKER, Dallas, Texas.

ALUM PRECIPITATED TOXOID IN DIPHTHERIA PREVENTION. THOMAS J. MCELHENNEY, Texas State J. Med. **30**:271 (Aug.) 1934.

McElhenney points out that, although the death rate from diphtheria is decreasing in the United States as a whole, it is increasing in Texas. He suggests that the reason for this is that a large part of the population is rural, and that the people have not been educated to the fact that children should be immunized in infancy rather than at school age.

Of 45 school children of Bessemer, Ala., who had positive Shick reactions before inoculation, all showed negative reactions one month after receiving one dose of alum-precipitated toxoid. The reactions were practically nil. The only objectionable feature has been the complaints of the mothers about the slow disappearance of the swelling. Of five hundred and fifty children of preschool age who gave strongly positive Schick reactions, all gave negative reactions five weeks after inoculation with 1 cc. of alum-precipitated toxoid. Only one had a febrile reaction, and that for but one day.

Because of the newness of the product, the author has no figures which suggest the duration of immunity. He believes that there should be no difference between the duration following this treatment and that of two doses of toxoid. He thinks that all children, no matter of what age, should be subjected to the Schick test before inoculation, because about 30 per cent are naturally immune.

MOORE, Dallas, Texas.

THE EXPERIMENTAL PRODUCTION OF MUMPS IN MONKEYS. G. M. FINLAY and L. P. CLARKE, Brit. J. Exper. Path. **15**:309, 1934.

Bacteriologically sterile saliva taken from a patient with mumps forty-eight hours after the onset and injected directly into Stensen's duct in rhesus monkeys produces a mild febrile reaction, swelling of the parotid glands and histologic changes very similar to those seen in human mumps. There is also a leukopenia. The virus has been passed through monkeys six times. It can be preserved in 50 per cent glycerin for at least five weeks. Injection of the virus into the tunica vaginalis of a monkey causes a nonsuppurative orchitis. Mice, rats and guinea-pigs inoculated intracerebrally did not present any symptoms.

AUTHORS' SUMMARY. [ARCH. PATH.]

AN UNUSUAL CASE OF DIPHTHERIA. JAMES GRANT, Brit. M. J. **1**:1074 (June 16) 1934.

Grant reports a case of primary diphtheria of the vulva without membrane in a 7 year old girl, followed by faucial diphtheria.

ROYSTER, University, Va.

TETANUS IN TOY-PISTOL WOUNDS. WILLIAM BROWN, Brit. M. J. **1**:1116 (June 23) 1934.

A case of tetanus following a wound from the blank cartridge of a toy pistol is reported. There follows a discussion on the incidence of tetanus following such wounds, with especial stress on the rarity with which Bacillus tetani is found in the wad or on the bullet.

WADDELL JR., University, Va.

MULTIPLE PERIPHERAL NEURITIS AS A COMPLICATION OF MEASLES. D. A. URQUHART, Brit. M. J. **2**:115 (July 21) 1934.

A case of multiple peripheral neuritis complicating measles is described. The picture of the patient is that of a very miserable creature. Thirty cubic centimeters of convalescent measles serum was administered, and there was apparently a rapid and prompt response. The author does not know whether the serum actually caused improvement or not.

ROYSTER, University, Va.

VARICELLA COMPLICATED BY TETANISM. THOMAS IMRIE, Brit. M. J. **2**:207 (Aug. 4) 1934.

Imrie reports a case of nervous phenomena resembling tetanus or tetanism. The former was ruled out of the diagnostic picture and the second diagnosis made.

ROYSTER, University, Va.

THE CONTROL OF DIPHTHERIA: A PLEA FOR ACTIVE IMMUNIZATION OF THE PRE-SCHOOL CHILD. W. T. BENSON, Edinburgh M. J. **41**:293 (May) 1934.

Benson compares the methods for the control of diphtheria in use in Edinburgh since 1912. He concludes that active immunization far excels the methods of passive immunization and the isolation of cases and carriers. During the past ten years since this type of immunization was begun there has been no apparent effect on the morbidity. He believes that if a course of three injections of toxoid were given to 50 per cent of Edinburgh's children from 1 to 10 years of age, there would be ample results in the lowering of the morbidity and mortality from diphtheria. Every effort should be made to immunize the children of from 1 to 5 years of age. At least 33 per cent of the children of this age should be made immune, and 50 per cent or more of the children of school age also, if a statistical effect on the morbidity is to be obtained.

Benson quotes some American and European statistics. It would seem that no country as yet has generally practiced this method of prevention to the degree that is more than a beginning.

NEFF, Kansas City, Mo.

THE VALUE OF THE "THICK FILM" METHOD IN THE DIAGNOSIS OF MALARIA. A. C. UKIL and S. C. CHOWDHURY, J. Indian M. A. **3**:528 (Aug.) 1934.

The authors were able to give a definite diagnosis of malaria by the examination of thick film preparations in 60 per cent of cases in which negative results were obtained by examination of thin film preparations. The technic employed in the use of the thick film preparations is described.

GONCE, Madison, Wis.

ACTIVE IMMUNIZATION AGAINST DIPHTHERIA. SHELDON F. DUDLEY, PERCIVAL M. MAY and JOSEPH A. O'FLYNN, Medical Research Council, Spec. Rep. Ser. no. 195, 1934.

This report is based on the research work done on the problem of diphtheria at the Greenwich Hospital School for boys during the past twelve years. The study is noteworthy not only for its comprehensiveness but also because during the first seven years of the study Schick tests were done and cultures from the throat were taken, but no active immunization was permitted. An unusual opportunity for comparative studies was offered when active immunization was begun as a routine five years ago. A great many interesting facts concerning immunity and carriers were disclosed by the investigation. Every physician who deals with children confined in institutions should read this monograph in the original. Only a few of the authors' findings and conclusions can be cited here.

Three years' residence in a community where diphtheria was endemic was accompanied by the development of as high a frequency of immunity as tested

by the Schick test as three doses of toxoid can produce in three months in the same community. The natural process was, of course, accompanied by a high morbidity. The rate of acquiring natural immunity as shown by the Schick test varied with the prevalence of diphtheria bacillary infection. After artificial immunization of the pupils higher rates were recorded for carriers of the virulent form than had ever been obtained before. A carrier state of the virulent form can sometimes exist for some weeks with a positive Schick reaction. At the end of 1932 the immunity of 10 per cent of those artificially immunized from six months to four years previously, as tested by the Schick test, was found to have relapsed, while only 3 per cent of those who had entered the school with immune Schick reactions were found to be susceptible, according to the Schick test. The carrier rate for the virulent form was lower than the expected rate in boys who had been tonsillectomized.

LEMASTER, Evanston, Ill.

EXPERIMENTAL DIPHTHERITIC PARALYSIS. G. RAMON, ROBERT DEBRÉ and PIERRE UHRY, Ann. Inst. Pasteur **52**:5, 1934.

The paralyzing effect of mild doses of diphtheria toxin or of doses of partially detoxified toxin on animals has long been known. The typical reaction in a guinea-pig is an ascending paralysis which may eventually result in death from cardiopulmonary complications. In rabbits paralysis was noted, but was similar to that noted with other bacterial toxins. The dog reacted in much the same way as the guinea-pig. The delayed paralytic reaction occurred simultaneously with antitoxin in the blood serum. Antitoxin was effective only when administered well in advance of the fixation of toxin by nerve tissues Methenamine, sodium salicylate, thyroxin and methylthionine chloride (methylene blue) failed to prevent paralysis. The symptoms were considered to be due to typical toxin. Results depended solely on the dosage. The fixation of toxin by nerve tissues seemed to occur within less than twenty-four hours after injection, although paralysis did not ordinarily appear before the third week.

M. S. MARSHALL. [ARCH. PATH.]

RARE LOCALIZATIONS OF DIPHTHERIA. P. EIVINE and N. SCHOENBAUM, Arch. de méd. d. enf. **37**:337 (June) 1934.

In spite of brilliant advances in the conquest of diphtheria, important problems remain. The malignancy in certain epidemics and the irreducible mortality and morbidity rates still constitute a challenge.

The authors report from the municipal quarantine service of Kiev, Russia, for a period of four months in 1933, a series of 91 cases in which the site of infection was unusual. These were distributed as follows: the skin, 25; the eyes, 14; the ears, 3; the nose, 34; the pharynx, 3; the buccal mucosa, 2; the vagina, 10.

The relative frequency (27.5 per cent) of diphtheria of the skin is a striking feature of this report. In contrast, Reiche of Hamburg found but 44 cases in a series of 7,314, and Adler, of Schick's clinic, but 23 cases among 2,217. It is pointed out that diphtheria of the skin was described by Paracelsus in 1566, and that its detection is a vital obligation for the epidemiologist.

A number of the cases are discussed in detail.

AMESSE, Denver.

DIET IN TYPHOID FEVER. N. Z. OUMIKOFF, Arch. de méd. de enf. **37**:351 (June) 1934.

The conviction that the diet of children stricken with typhoid should be confined exclusively to liquids is still strongly held by many physicians and by practically all laymen. In view of the easily attested fact that this infection is apt to be much less severe in the young than in adults and that abortive cases are common and complications rare, the author, writing from Tiflis, calls attention to the loss of appetite attending the monotonous liquid ration ordinarily employed in these

cases and expresses himself in favor of a mixed diet, fairly rich in proteins, fats and carbohydrates. His experience with 429 cases is recounted.

AMESSE, Denver.

ENCEPHALITIC COMPLICATIONS OF SCARLET FEVER. R. HUBORIS, Rev. franç. de pédiat. **10**:320, 1934.

Two cases are presented as examples of the acute ataxia of Leyden developing during the course of scarlet fever. The first case is that of a girl, 5 years of age, previously normal, who had mild scarlet fever and who showed the following neurologic picture: For five days she was acutely ill, with loss of memory, inability to sit or stand, incontinence, nystagmus, abnormal movements of the right arm and a positive Babinski sign on the right. These symptoms cleared to reveal a marked cerebellar ataxia predominantly of the right side. By the fortieth day this had disappeared except for slight disturbance in the right arm and slow and monotonous speech. After a year and a half the picture is about the same, and a moderate degree of mental retardation is present.

The second case is that of an 18 year old girl, who had always showed marked mental retardation. During scarlet fever the following developed: marked cerebellar ataxia, strictly localized to the right side, and paralysis on the right side due to pyramidal involvement; hypotonia, with exaggeration of reflexes; a positive Babinski sign, and ankle and patellar clonus. She also had disturbance of speech and ocular movements and laughed and cried with no cause. There was gradual improvement in her condition, but the pyramidal involvement has persisted up to the fourth month following the onset of the acute illness.

LESLIE, Evanston, Ill.

ANTITYPHOID VACCINATION OF CHILDREN: METHODS. L. TANON and H. CAMBESSÉDÈS, Rev. franç. de puériculture **2**:129 (June) 1934.

All children should be vaccinated against typhoid. Under normal conditions vaccination by mouth may be used. Where there is known danger of infection vaccination by injection is surer. A higher proportion of immunity is obtained by using the watery suspension for injection in fractional doses than by using the suspension in oil in a single dose. Severe reactions can be avoided by testing the sensitivity of the patient in advance and modifying the size and number of doses accordingly.

CRANE, Chicago.

EPIDEMIOLOGY OF DIPHTHERIA IN THE PROVINCE OF PIACENZA. A. MANARINI, Prat. pediat. **12**:243 (June) 1934.

This is a brief statistical review of the cases of diphtheria in patients admitted to the Civil Hospital in the past decade. The pharyngeal and laryngeal types were almost equally present in about three hundred and thirty-one cases. There was a gradual increase in the incidence of the disease until 1930, the peak year, since which time there has been a gradual decline. The total mortality was 14 per cent; there was little variation from year to year. The mortality in the laryngeal form was about three times greater than that in the pharyngeal.

DOOLEY, New York.

PERMEABILITY OF THE BARRIER BETWEEN THE BLOOD AND THE SPINAL FLUID IN POSTDIPHTHERITIC PARALYSIS. V. MENGOLI, Riv. di clin. pediat. **32**:537 (May) 1934.

Mengoli made observations on the blood and spinal fluid of six children with postdiphtheritic paralysis. To get an index of the permeability of the blood-spinal fluid barrier to electrolytes, he compared the bromide content of the blood and of the spinal fluid. The quotient of permeability of the bromide in the blood and the bromide in the spinal fluid is normally between 2.9 and 3.3.

The contents of diphtheria antitoxin in the blood and spinal fluid were determined and compared, affording an index as to the permeability of the barrier to a colloid.

The results found are given in the following table:

Case	Bromide Quotient	Units of Antitoxin	
		In 1 Cc. of Blood Serum	In 1 Cc. of Spinal Fluid
1.	2.01	>1	1/100
2.	2.45	>1	1/100
3.	2.81	>1	1/250
4.	2.95	>1	1/600
5.	2.96	>1	1/500
6.	3.50	<1/100	>1/1,000

The more permeable the barrier is to bromide (an electrolyte), the more permeable it is to antitoxin (a colloid). In five of the six cases definite amounts of antitoxin were present in the spinal fluid.

HIGGINS, Boston.

INFECTIOUS ERYTHEMIA JOSÉ M. DA ROCHA, Arch. de pediat., Rio de Janeiro **6:** 677 (April) 1934.

The author presents a case of this condition in a child of 8 months. He reviews the literature and discusses the etiology and pathology. There are two photographs of his own patient and a colored plate. The incubation period is from six to seventeen days. The prodromal symptoms are anorexia, vomiting, fever and sometimes symptoms of a cold. The eruption appears first on the face and spreads over the whole body. It is by no means solid, but is slightly raised and liable to serpentine gyrations. There is no treatment, as the disease is self-limiting.

SANFORD, Chicago.

DIPHTHERIA. FELIX HURTADO, Bol. Soc. cubana de pediat. **6:**79 (May) 1934.

In spite of all the present-day knowledge of diphtheria, this disease is still prevalent and is still fatal, especially to the young infant.

Diphtheria must be diagnosed as early as possible and antidiphtheritic serum given promptly. No dosage of less than 5,000 units should be used at a time or as an initial dose, even in benign cases. The author advises against the promiscuous use of antidiphtheritic serum for anginas not due to the diphtheria bacillus, but advocates its use in doubtful cases or in cases in which there is difficulty in establishing the diagnosis promptly. In malignant cases of diphtheria the serum at times seems to be without effect. To guard against untoward effects of sensitization the author advises a careful check of the history with reference to the previous use of serums or vaccines, and in all doubtful cases desensitization should be practiced.

Constant propaganda should be carried on to effect complete immunization of the entire population against diphtheria.

SCHLUTZ, Chicago.

PRESENCE OF PSEUDODIPHTHERIA BACILLI IN THE SPUTUM OF MAN AND THE QUESTION OF THE MUTATION OF SUCH ORGANISMS INTO TRUE DIPHTHERIA BACILLI. H. LAUB, Arch. f. Hyg. **112:***222* (July) 1934.

Laub comments on the widespread distribution of pseudodiphtheria bacilli in man and animals. The methods of distinguishing between such bacilli and true diphtheria bacilli are discussed. Pseudodiphtheria bacilli were found in eighty of one hundred and forty specimens (76.8 per cent of cases) of sputum obtained from normal persons. Only seven of sixty-four cultures of pseudodiphtheria bacilli experimented with were so altered, after from forty-nine to eighty-eight transfers on blood agar, that their morphologic, staining and cultural characteristics could not

be distinguished from true diphtheria bacilli. None of these seven cultures, however, could be shown to be pathogenic for experimental animals.

GLASER, Rochester, N. Y.

EPIDEMIOLOGY OF SCARLET FEVER IN BRATISLAVA (PRESSBURG). A. J. CHURA and S. LIMBACHEROVA, Monatschr. f. Kinderh. **60**:9, 1934.

The authors review the records of the last fifty years, including reports of more than 7,300 cases of scarlet fever. Scarlet fever does not resemble diphtheria in epidemiology. Epidemics of diphtheria are relatively short. At no time during these fifty years did an epidemic of scarlet fever occur simultaneously with an epidemic of diphtheria. The epidemics of scarlet fever seemed to arise with the decline of the diphtheria epidemics, but lasted much longer.

The mortality of scarlet fever has declined markedly. About twenty years ago it was as high as 26 per cent. In recent years it has been down to zero. There is no parallelism between the authors' figures and those of other cities in which the mortality per hundred thousand varied from 77 in Leningrad to 0.7 in Brussels. Diphtheria seems to affect younger children, while scarlet fever is preeminently a disease of school age.

The authors conclude that there are unknown factors in the epidemiology of scarlet fever and that the curve cannot be plotted with the accuracy of that of diphtheria.

GERSTLEY, Chicago.

CHILDREN AS TYPHOID AND PARATYPHOID BACILLI CARRIERS. F. LAESSING, München. med Wchnschr. **81**:783 (May 25) 1934.

Thirty patients with typhoid and eighty-eight children with paratyphoid admitted to the hospital over a period of five years were studied. About one third of the patients with typhoid were children. Infants may contract typhoid or paratyphoid. The younger the patient the more difficult the diagnosis. Children, just as adults, may continue to excrete bacilli for a short or long period after recovery from the acute illness. Prolonged excretion of bacilli occurs more often after paratyphoid than after typhoid. Laessing makes a distinction between carriers and those who continue to excrete bacilli after having the clinical manifestations of the disease. Carriers are those who have had an abortive or undiagnosed attack of typhoid or paratyphoid. Children are frequently carriers and may easily become an important source of infection

BRAHDY, Mount Vernon, N. Y.

BIOLOGY OF DIPHTHERIA EPIDEMICS. RUDOLF UHLIRZ, Wien. klin. Wchnschr. **47**:615 (May 18) 1934.

Uhlirz states that the following phenomena proceed according to biologic rules: 1. Carriers of latent, avirulent diphtheria bacilli (type A) fall ill with diphtheria after tonsillitis, scarlet fever or measles. Type A, the avirulent bacillus, leads to disease because of the greater disposition of the tissue to illness and becomes type B, the virulent type. 2. Persons become ill after tonsillitis, scarlet fever, measles and other diseases by infection from carriers of type A diphtheria bacilli. 3. Diphtheria often fails to appear in persons with healthy throats, and they become carriers of type A bacilli. The necessary biologic conditions for an epidemic of diphtheria are to be found in all the circumstances which lead to an increase of the type B bacillus or to increased disposition to the disease. There may be direct infection of healthy persons because of lack of early isolation, or diphtheria may occur in connection with an epidemic of scarlet fever, measles or tonsillitis. The time of year affects the number of cases of diphtheria; at certain times, especially in winter, there is increased disposition to disease on account of lowered resistance.

ABT, Chicago.

FURTHER EXPERIENCES WITH LÖWENSTEIN'S DIPHTHERIA SALVE. JOSEF SIEGL and NATALIE DRACH, Wien. klin. Wchnschr. **47**:965 (Aug. 3) 1934.

Siegl and Drach report on the use since 1931 of Löwenstein's ointment in the children's clinic of the University of Vienna. The ointment was well rubbed into the back over a large area, and this procedure was repeated twice with intervals of one week between treatments. In 222 children who were thus treated with the ointment the Schick test was undertaken from six to eight weeks after the last treatment. In 97 children the reaction became negative, and in 125 it remained positive; i. e., the ointment was effective in 43.7 per cent of the cases. On the basis of their experiences, the authors state that marked hopes of improvement of this method of diphtheria prophylaxis have not been fulfilled. On the contrary, the ointment preparations given out since 1930 (that given out in 1930 by Löwenstein appears to have been the most effective) have had poorer immunizing effect than the previous ones. The prospects of a practical evaluation of this method have sunk considerably. It is also noted that the immunity obtained by Löwenstein's ointment is of shorter duration than that obtained by other methods.

ABT, Chicago.

SEPSIS AFTER SCARLET FEVER AND DIPHTHERIA AND ITS TREATMENT. H. CLAUS, Ztschr. f. Laryng., Rhin., Otol. (Teil 1: Folio oto-laryng.) **25**:8, 1934.

Sepsis, according to Claus, in the sense of Schottmüller, means a periodic or continuous invasion of the blood stream by pathogenic organisms from a focus, from which objective and subjective signs of generalized illness result. Though this condition is relatively rare in scarlet fever, it occurs. The author cites six such cases involving venous thrombi in patients on whom he was called to operate. Thrombi were found in one or more of the jugular or facial veins and treated by ligature above and below. Recovery occurred in four cases and death in two. In the fatal cases, however, it was not possible to isolate the thrombi successfully. A similar mixed infection thrombus developed in a patient with diphtheria in whom infarction of the lung had already occurred. There was eventual recovery. Although this procedure is not a common necessity, the author thinks that it promises the saving of some patients with otherwise hopeless conditions.

EDITOR'S ABSTRACT. [ARCH. OTOLARYNG.]

Chronic Infections

PRACTICAL CLINICAL AND LABORATORY ASPECTS OF PRECIPITATION TESTS FOR SYPHILIS. E. B. RITCHIE, RUTH HERRICK and J. M. VAN DE ERVE, Arch. Dermat. & Syph. **29**:835 (June) 1934.

This article includes a discussion of the theoretical basis on which the precipitation and complement-fixation tests rest. The following precipitation tests are given in detail: Kahn, Hinton, Müller ball, Kline and Rosenthal. A comparison of the value of the tests is made based on (1) specificity, (2) simplicity, (3) rapidity of performance and (4) purposes of usage. The authors found the Hinton, Kline and Rosenthal tests all satisfactory but did not think that any one had advantages over the Kahn test, which they had been using previously. The importance of doing both a complement-fixation and a precipitation test on all serums in question is emphasized.

DULIN, Iowa City.

TREATMENT OF RESISTANT SOMATIC SYPHILIS. CHARLES C. DENNIE and W. L. MCBRIDE, Arch. Dermat. & Syph. **30**:1 (July) 1934.

Malarial therapy is advised in the treatment of resistant somatic syphilis. Resistant cases of somatic syphilis that do not respond to the routine therapy do not reflect the inefficiency of arsenic, bismuth or mercury preparations or iodides but the failure of the defense mechanism of the body. This defense mechanism

may be again activated by malarial therapy, heat therapy or the administration of typhoid vaccine, the efficiency being in the order named. Heat, it is believed, is only an activating factor and does not destroy the organisms of syphilis. Malaria enhances the value of subsequent treatment, but if the treatment is used too soon it may precipitate the original condition. DICK, Iowa City.

USE OF CONCENTRATED DIET IN CHILDHOOD TUBERCULOSIS AND MALNUTRITION. GERALD E. PRATT, Arch. Pediat. **51**:529 (Aug.) 1934.

In the treatment of the childhood type of tuberculosis, dietary requirements are higher than in the normal child, as to both the quantity and the quality of food. A group of forty undernourished children, thirty-five of whom had a positive Mantoux reaction, were given a reenforced diet, which resulted in gratifying gains in weight and general improvement in the physical condition. Powdered whole milk was used to supplement the daily diet. The advantages of this product are its cleanliness and bacterial safety, its easy digestibility, its high nutritive value and the fact that it may be incorporated in powder form in other foods without appreciable effect on their flavor, texture or bulk. Powdered whole milk is a valuable adjunct in the dietary treatment of the childhood type of tuberculosis and in malnutrition and undernourishment. WADDELL JR., University, Va.

THE VALUE OF STOVARSOL IN THE TREATMENT OF SYPHILIS. WALTER WILHELMJ, Illinois M. J. **65**:553 (June) 1934.

Wilhelmj believes that the peroral administration of acetarsone is the treatment of choice in cases of syphilis in children. BARBOUR, Peoria, Ill.

PREVENTION OF CONGENITAL SYPHILIS. JACOB A. GOLDBERG, New York State J. Med. **34**:290 (April 1) 1934.

This article is part of a symposium on syphilis. A study of 653 cases of prenatal syphilis in 7 prenatal clinics in New York City is reported on. Only 22.5 per cent of the patients were put under treatment before the fifth month of pregnancy. Better attention to this condition would reduce both the mortality and the morbidity in this condition. AIKMAN, Rochester, N. Y.

DIAGNOSIS, IMPORTANCE, AND TREATMENT OF EARLY SYPHILIS. GEORGE M. MACKEE, New York State J. Med. **34**:293 (April 1) 1934.

This article is part of a symposium presented at the annual meeting of the Medical Society of New York County. AIKMAN, Rochester, N. Y.

THE INTRADERMAL TUBERCULIN REACTION WITH SPECIAL REFERENCE TO SO-CALLED SURGICAL TUBERCULOSIS. J. W. E. CORY, Arch. Dis. Childhood **9**:177 (June) 1934.

In a study of the intradermal tuberculin reaction in various groups of cases, the test was found more accurate in disease of the bones and joints than in other conditions, with the possible exception of glandular disorders.

In the whole series eighty-four tuberculous patients gave positive skin reactions, and one hundred and thirty-one nontuberculous patients gave negative reactions. In seventeen cases the skin reaction was negative and the tentative diagnosis had to be revised, while in another seventeen cases the skin reaction was positive without tuberculosis being the cause of the pathologic condition for which the patient was under treatment. In five cases of tuberculosis the reaction was negative.

The positive intracutaneous reaction means that the child has acquired a definite allergic reaction to the products of the tubercle bacilli and either has or has had tuberculosis. Children whose parents are tuberculous and who are exposed to open tuberculosis at home are much more liable to produce a positive reaction, although they may not be suffering from active tuberculosis at the time.

There seems to be little doubt that the younger the child the greater must be the significance attached to a positive result, and that the older the child the less importance need be attached to it from a clinical aspect. The intradermal test, therefore, should never be allowed to establish a diagnosis of tuberculosis unless well supported by other evidence, but the test should take its place, and a very useful place, in the balance of evidence for or against a diagnosis of tuberculosis.

KELLY, Milwaukee.

THE DIAGNOSTIC AND THERAPEUTIC USE OF TUBERCULIN IN CERTAIN OCULAR CONDITIONS. GORDON B. FLINT, Tr. Med.-Chir. Soc. Edinburgh, 1933-1934, p. 93; in Edinburgh M. J., July 1934.

To determine whether the Continental opinion is correct that many chronic inflammatory conditions of the eye—iritis, iridocyclitis, choroiditis and scleritis—may be due to tuberculosis, Flint studied the clinical appearance and course of such a disease; he further tried to exclude syphilis and focal infection, and finally did the routine tests with a tuberculin preparation used in recent years in Vienna. The intradermal method was used. Three injections ranging from 0.000001 to 0.0001 mg. were made into one arm; these were repeated if the reaction was negative, at two sites on the other arm, in doses of 0.001 and 0.01 mg. There is no trauma to the eye with this material, an accident which is said to have happened with old tuberculin.

Therapeutic doses are given biweekly to the reactors, in beginning doses equal to that which causes a reaction; the amount is increased 50 per cent until a dose of 0.05 mg. is reached, and this dose is continued for one year or more.

The illustrative cases cited are in adults. Flint believes that more time and extended experience with tuberculin in these diseases of the eye are needed before one can share the enthusiasm of Vienna observers, but that the reaction to the tuberculin preparation is of diagnostic value when correlated with a positive history of tuberculosis, and, finally, that a satisfactory result follows the therapeutic use of this tuberculin.

NEFF, Kansas City, Mo.

A STUDY OF THE OCCURRENCE OF VIRULENT TUBERCLE BACILLI IN THE EXCRETA OF TUBERCULOUS INDIAN CHILDREN. A. B. SIMES and L. E. PAYNTER, Tubercle **15**:498 (Aug.) 1934.

Two groups of Indian boarding-school children were examined by these Canadian observers to determine by inoculation of guinea-pigs the infectivity of the urinary and fecal excreta. Group one consisted of tuberculin-sensitive children who presented no demonstrable tuberculous lesions. No tubercle bacilli were present in the excretions of these children. Group two had definite pulmonary lesions which were apparently closed. They were well nourished and without respiratory symptoms. They were classified in three divisions: (*a*) those with closed pulmonary infection with inactive lesions; (*b*) those with closed infection with pulmonary lesions considered active from roentgen evidence only; (*c*) those with closed infection with active pulmonary lesions shown by roentgen examination and clinical symptoms. Of the forty children in this group, 20 per cent were excreting virulent tubercle bacilli in the feces, and 12.5 per cent, in the urine. None of the children had any symptoms of intestinal tuberculosis. Segregating this group into the three divisions just indicated, in the first division five had virulent tubercle bacilli in the excreta; in the second division one had infective excreta, and in the third division five had infective excreta.

The finding of virulent tubercle bacilli in 27.5 per cent of this group of children indicates that unhealed tuberculous lesions of the lungs are a source of infection, whether the lesions are clinically active, active as shown roentgenologically or healing, although the disease may be minimal in extent, with no cavities demonstrable and no sputum present apart from that associated with colds and nontuberculous respiratory infections.

EUGENE SMITH, Ogden, Utah.

SEROLOGIC VALUE OF "TUBERCLE DE CARABELLI AND SABOURAUD" IN HEREDITARY OCULAR SYPHILIS. E. AUBINEAU, Ann. d'ocul. **171**:671 (Aug.) 1934.

In syphilis, particularly in hereditary syphilis, it is the clinical examination which forms the primary guide of the practitioner. A positive Wassermann reaction is an argument in favor of syphilis, but this serologic reaction is so often negative in hereditary syphilis that too much dependence on it is dangerous not only for the patient but for his family and even for the physician.

The importance of syphilis in ocular pathology has been called to the attention of physicians by the communications of Sabouraud which appeared in *La presse médicale* in 1917, by the thesis of Lefebvre in 1920, and by the articles of Hissard in 1930 and by Lamache in 1931.

The following clinical observations are detailed: Among 2,600 children between the ages of 8 and 13 years who presented themselves from 1924 to 1933, there were 91 carriers of "tubercles of Carabelli and Sabouraud." This percentage corresponded with that of Hissard (4 per cent). Among these 91 children presenting dental dystrophy there were found 73 with ocular involvements. The details of this observation are given in table form.

MCKEE, Montreal, Canada. [ARCH. OPHTH.]

CRYSOTHERAPY IN PULMONARY TUBERCULOSIS. W. JULLIEN, Paris méd. **2**:127 (Aug. 18) 1934.

Jullien claims good results from intravenous injections of gold and sodium thiosulphates in the treatment of recent ulcerative tuberculosis in young persons. In older, debilitated patients he uses oil suspensions of the same salts intramuscularly. He does not give any details of treatment.

LESLIE, Evanston, Ill.

VALUE OF CERTAIN SYMPTOMS OF TUBERCULOSIS OF THE TRACHEOBRONCHIAL LYMPH NODES IN INFANTS. A. S. LEVINE, Rev. franç. de pédiat. **10**:241, 1934.

The difficulties in the diagnosis of tuberculosis of the tracheobronchial lymph nodes are discussed. D'Espine's sign and Carany's sign are by no means exact. An expiratory whistle may indicate pressure on the trachea. Emphysema may indicate pressure or encroachment on the bronchus which does not produce complete obstruction but allows air to enter but not to escape. Roentgen therapy is of doubtful value. Enlargement of the lymph nodes is not always tuberculous, but evidence of enlargement together with a positive Mantoux reaction is presumptive evidence of the tuberculous nature of the process, and treatment and change of environment should be directed accordingly.

LESLIE, Evanston, Ill.

BRONCHOPULMONARY SYPHILIS IN INFANCY. M. PÉHU and JEAN ROUGIER, Rev. franç. de pédiat. **10**:257, 1934.

The authors point out that disorders of the lung due to congenital syphilis divide themselves into three groups: (1) In the fetus and the new-born they are represented by pneumonia alba and gummas of varying degree and extent. Death occurs in utero or shortly after birth, and other manifestations of syphilis are usually present. (2) In the second period of childhood, that is, after the third

year, one observes by functional signs and by roentgenograms dilatation of the bronchi of the type described by Laënnec. (3) In the period between these two, that is, during the first three years of life, the syphilitic pneumopathy is neither pneumonia alba nor classic bronchial dilatation. The diagnosis is difficult, and in the majority of cases there are no clinical signs, but autopsy reveals small bronchial dilatations, interstitial bronchopneumonia and perivascular or interlobular sclerosis. The roentgen rays may show diffuse, poorly defined shadows or exaggeration of the vascular tree. Other patients may show exaggerated hilar shadows due to sclerosis of the arteries, which resemble in roentgen appearance tracheobronchial adenopathies. Others may give the pictures of cysts of the lung. In six of the fourteen cases encountered in the course of eleven years the patients showed cyanosis, clubbing of fingers and toes and cough. These cases must be differentiated from those of chronic bronchitis and from those of tuberculous bronchopneumonia. The conditions are difficult to differentiate by the roentgen rays alone. The tuberculin test and the temperature curve will help. In the syphilitic pneumopathies there is no elevation of temperature.

LESLIE, Evanston, Ill.

INFLUENCE OF ULTRAVIOLET RAYS ON THE IMMUNITY REACTIONS TOWARD TUBERCULOSIS. MARCELLA PIA LEBAN, Riv. di clin. pediat. **32**:587 (May) 1934.

Seventy-six children with positive tuberculin reactions were irradiated, thirty by the quartz mercury vapor lamp and forty-six by heliotherapy. The effects of irradiation on the tuberculin reaction were studied. One arm was protected from irradiation in each child, tuberculin tests being made on both the irradiated and the nonirradiated arm.

Thirty children were irradiated by the mercury vapor lamp. The tuberculin reaction became negative in five children on both arms, in twelve on the irradiated arm and in six on the nonirradiated arm; it became attenuated in nine children on the irradiated arm and in sixteen on the nonirradiated arm. In no child was the reaction on the irradiated arm so marked as before irradiation, although on the nonirradiated arm no change was noticed in seven children. Subsequent tests after a period of time showed a tendency for the skin reaction to return to its previous intensity.

Forty-six children were tested before and after a course of heliotherapy extending over a period of from 1,800 to 5,645 minutes. The tuberculin reaction become negative on both arms of eleven children; it became negative on the irradiated arm of forty-two children and on the nonirradiated arm of eleven children; it showed attenuation on the irradiated arm of four children and on the nonirradiated arm of thirty children and showed no change in intensity on the nonirradiated arm of five children.

Most of the children had tuberculous adenitis.

HIGGINS, Boston.

PRETUBERCULOSIS. G. FIORE, Riv. di clin. pediat. **32**:641 (June) 1934.

Fiore reviews the recent literature regarding the virus of tuberculosis (virus of Fontes-Koch). Tuberculous infection must be regarded as due not solely to the bacillus of Koch but also to a virus passing through various forms until it arrives at the classic bacillus of Koch. Tuberculous disease is not only an expression of the action of the bacillus of Koch and its toxin but also an expression of the tuberculous virus and of protogenic tubercle bacilli. The protogenic tubercle bacilli have a specific affinity for the lymphatic system, provoking a disease susceptible of cure, which does not necessarily cause sensitivity to tuberculin and produces more or less immunity toward the Koch bacillus. A clinical syndrome pretuberculosis due to the tuberculous "protogenes" may be recognized to affect the lymphatic system of children; it may mark the beginning of classic tuberculosis or of satisfactory immunity.

HIGGINS, Boston.

REACTION OF TUBERCULIN COVERED WITH COURT-PLASTER. J. M. SALA GINABRÉDA, An. de pediat. **1**:282 (May) 1934.

The author investigated the reaction obtained when tuberculin is placed on the skin and covered with court-plaster. The technic of the reaction is as follows: The forearm is the site of choice. This area is cleansed with ether; then a drop of tuberculin is placed on the skin and is covered with a piece of court-plaster about 3 cm. square. Care is taken that the court-plaster is adherent at its borders. Alongside this patch another patch of court-plaster the same size is placed as a control. The reaction is read in forty-eight hours. When the reaction is positive there appears under the tuberculin square a fine papular or papulovesicular eruption on an erythematous base. The erythema does not disappear on pressure. If the person is not sensitive to court-plaster the skin under the control patch shows no reaction. Even if the skin is sensitive to the plaster and erythema is produced, it is easily differentiated from the true positive reaction. The erythema in the false test disappears on pressure and does not produce papules or vesicles. This reaction is not as sensitive as the Mantoux reaction, the latter being positive in 7 per cent more instances in the author's series of one hundred cases.

HERRON, Spokane, Wash.

JUVENILE TABES. RAUL C. AGUIRRE and RODOLFO TETES, Arch. argent. de pediat. **5**:177 (April) 1934.

The authors report the occurrence of this rare condition in a child aged 9 years. Syphilis in their case was congenital and not acquired. The patient showed many of the classic symptoms of tabes, such as optic atrophy and loss of the patellar and the achilles tendon reflex. Urinary incontinence was pronounced, and there were frequent recurrent attacks of gastric crises. The spinal fluid showed the characteristic changes of tabes. The pupils showed the typical Argyll Robertson reaction. Arsenic and bismuth preparations alternating with mercurials were used in the treatment. The authors are under the impression that retardation and partial arrest of the condition can be obtained with this form of therapy.

SCHLUTZ, Chicago.

SECONDARY PERIFOCAL INFILTRATIONS IN CHILDHOOD. JOSÉ MARIA MACERA and ELIAS PITERBARG, Arch. argent. de pediat. **5**:297 (June) 1934.

This condition has been described under a variety of names, such as epituberculosis, splenopneumonia chronica tuberculosa, splenopneumonia of Bourdet, massive pneumonia of Crancher, paratuberculosis of Engel and perifocal infiltration of Redeker. The latter term is most widely accepted. Careful roentgenologic examination, various biologic tests and the course and development differentiate it from true mediastinal tuberculosis.

SCHLUTZ, Chicago.

DIAGNOSIS OF SYPHILIS FROM A DROP OF DRIED BLOOD. PETER DAHR and REINER MUELLER, Arch. de med. inf. **3**:737 (June) 1934.

When the findings in 600 routine tests were compared with the reactions obtained with the method of Chediak (described in volume 2 of the *Archivos de medicina infantil*, 1933), who employs a drop of defibrinated and desiccated blood on a slide, the usefulness of this method was proved. The simple procedure for obtaining blood permits the practitioner to carry out tests for syphilis in nurslings, young infants and obese persons. It is also useful in places where the laboratory is at some distance.

SANFORD, Chicago.

THE SCHOOL, AN IMPORTANT FACTOR IN PROPHYLAXIS OF JUVENILE TUBERCULOSIS. JESUS A. FIGUERAS, Bol. Soc. cubana de pediat. **6**:71 (May) 1934.

Figueras discusses the great possibilities of vaccination with the Calmette-Guérin bacillus as a protective measure against tuberculosis. During the school

age additional agencies must be supplied. Among these are fresh air schools, physical education, spring colonies, colonies on the seashore and school lunches. For children definitely affected with tuberculosis the author advises the establishment of open air schools, dispensaries for their treatment and education in proper hygiene. He also advises the building of pavilions at low cost for housing the tuberculous children.

SCHLUTZ, Chicago.

THE INFLUENCE OF SYPHILIS ON PREGNANCY AND THE TREATMENT OF THE PREGNANT SYPHILITIC MOTHER. AVILES, Rev. chilena de pediat. **5**:222 (April) 1934.

Syphilis not only has a direct toxic action on the fetus but has an equally deleterious action on the fetal adnexae, particularly the placenta. The earliest possible treatment of the pregnant syphilitic mother is an absolute necessity. Of the three therapeutic remedies, mercury is now seldom used, as its action is not rapid enough. Arsenicals have been in great favor and are extensively used but are not without danger in massive dosage. Bismuth preparations are preferred above all other forms of treatment. The method of administration is convenient and easy, and the results are satisfactory. On the whole, the bismuth preparations are somewhat less effective than the arsenicals. It is often well to combine the two in the treatment of resistant conditions.

SCHLUTZ, Chicago.

TUBERCULOUS LUNG INFILTRATION AND CARBOHYDRATE METABOLISM IN CHILDHOOD. H. VON METTENHEIM, Med. Klin. **30**:1020 (Aug. 3) 1934.

Dextrose tolerance tests (using 2 Gm. per kilogram of body weight) were performed on eighty-eight tuberculous children who ranged in age from 4 months to 13 years but were chiefly under 3 years of age. The absolute values during fasting in tuberculous children averaged somewhat (from 80 to 88 mg. per hundred cubic centimeters) higher than in normal children. There was a shift in the hyperglycemic quotient, i. e., the relationship between the highest point on the curve and the initial point, in tuberculous children. In tuberculous infiltration the quotient was from 1.69 to 1.7; in hilus gland tuberculosis, 1.77; in extrapulmonary tuberculosis, 1.45; in phthisis, 1.43, and in normal children, 1.34. Tuberculous children also showed a delay in the return to the initial values (more than two and one-half hours as compared with two hours in normal children).

DOOLEY, New York.

Internal Diseases

INCIDENCE AND SIGNIFICANCE OF ACTIVE INFECTION IN CASES OF RHEUMATIC CARDIOVALVULAR DISEASE DURING THE VARIOUS AGE PERIODS: A CLINICAL AND PATHOLOGICAL STUDY. M. A. ROTHSCHILD, M. A. KUGEL and LOUIS GROSS, Am. Heart J. **9**:586 (June) 1934.

The authors report a clinical and pathologic study of 161 persons dying with evidence of rheumatic heart disease. Of the total number studied, 106 showed anatomic evidence of active infection, while in 55 the disease was quiescent. Twenty-two children succumbed during the first decade of life, and all these showed active infection. In the second decade 95 per cent, in the third decade 78 per cent and in the fourth decade 70 per cent revealed signs of activity. In the age groups beyond 40, the precentage dropped sharply but was still unexpectedly high.

Of 106 patients in whom active lesions were found in the myocardium 103 died of circulatory failure. Of 55 in whom no evidence of active infection was detected 35 died of circulatory failure or its complications.

The occurrence of heart failure in persons under 40 years of age who have a valvular defect in the great majority of instances may be attributed to an active infection of the myocardium rather than to the degree of the mechanical defect.

GIBSON, Chicago.

SOME OBSERVATIONS ON FOOD ALLERGY. WARREN T. VAUGHAN, Am. J. Digest. Dis. **1**:384 (Aug.) 1934.

Vaughan brings out the importance of food allergy in general medicine, particularly in regard to gastro-enterology. He emphasizes the fact that skin tests are only the beginning of a diagnostic allergy study. This study, of course, requires the most painstaking efforts and collaboration on the part of both the physician and the patient and is often not completed until after months of study. He calls attention to the fact that mere routine histories often cause the physician to overlook foods or pollens to which the patient may be sensitive. He advocates a thorough discussion with the patient, usually outside the domain of the physician's office, and states that one of the best ways of finding what a person is sensitive to is by eating a meal with him. This is particularly true in regard to the patient who is a chronic invalid.

MORRISON, Savannah, Ga.

REVISED ELIMINATION DIETS FOR THE DIAGNOSIS AND TREATMENT OF FOOD ALLERGY. ALBERT H. ROWE, Am. J. Digest. Dis. **1**:387 (Aug.) 1934.

Rowe suggests the use of elimination diets as aids in the diagnosis and treatment of food allergies. Certain symptoms of suspected food allergies may be studied with the elimination method of diet after test diets have given negative results. Whenever possible, the diet should be modified for positive skin reactions by routine testing with food allergens and by histories of unfavorable reactions to food. It is justifiable to use the elimination diets modified only by the history of food idiosyncrasies with skin tests, if such tests are available. A complete list of elimination diets are submitted.

MORRISON, Savannah, Ga.

CHRONIC HEREDITARY HEMOLYTIC JAUNDICE WITH REPORT OF 8 CASES AND NOTES ON MEASUREMENT OF THE SIZE OF ERYTHROCYTES. WILLIAM FITCH CHENEY and GARNETT CHENEY, Am. J. M. Sc. **187**:191 (Feb.) 1934.

Three cases of chronic hereditary hemolytic jaundice in one family are reported, with reports of five other cases. The patients were from 40 to 67 years of age, with the exception of one patient, the third member of the aforementioned family, who was 4 years of age. The article is lengthy and embraces the history, incidence, etiology, pathology (liver, spleen, bone marrow and other organs), clinical history, complications, physical examination, laboratory tests (the number of red cells and their size, the reticulocytes, the increased fragility of the red cells, the white blood cells, the blood serum, the urine and the feces), diagnosis and treatment.

It is stated that the occurrence of pronounced microcytosis in the presence of jaundice, whether clinical or latent, may be considered almost diagnostic of chronic hereditary hemolytic jaundice. The red cells have a lessened resistance to hypotonic salt solution.

HENSKE, Omaha.

INTESTINAL ACARIASIS DUE TO TYROGLYPHUS LONGIOR GERVAIS. E. HAROLD HINMAN and R. H. KAMPMEIER, Am. J. Trop. Med. **14**:355 (July) 1934.

Hinman and Kampmeier review briefly the literature on the mites of the family Tyroglyphidae and report two cases of intestinal acariasis occurring in man, one in a child and the other in an adult. They also experimented with dogs to determine whether these mites could produce diarrhea in a normal dog, without results.

The failure was thought to be due to the resistance of the individual dog to the mites, or to the fact that an insufficient number of mites were ingested.

BURPEE, Augusta, Ga.

MUSCULAR DYSTROPHY AND ATROPHY: CLINICAL AND BIOCHEMICAL RESULTS FOLLOWING THE ORAL ADMINISTRATION OF AMINO-ACIDS. CARLO J. TRIPOLI and HOWARD H. BEARD, Arch. Int. Med. **53**:435 (March) 1934.

In treating patients with various forms of muscular atrophy and dystrophy with amino-acids, Tripoli and Beard prefer glutamic acid to glycine because the former constitutes a larger proportion of muscle protein than glycine and because it is cheaper, less toxic and more efficient in forming creatinine. They classify these disorders into the primary muscular myopathies and progressive nuclear muscular atrophy, the latter including progressive spinomuscular atrophy, posterolateral sclerosis and bulbar palsy. Six cases are presented, three in each group. The patients in the second group were classified as follows: (1) a patient with progressive spinomuscular atrophy who showed some improvement in muscular strength and diminution in twitchings following a course of treatment with glycine (10 Gm. daily); (2) a patient with amyotropic lateral sclerosis who showed slight improvement in muscle tone following oral administration of glutamic acid (10 Gm. daily in milk), and (3) a patient suffering from amyotropic lateral sclerosis who showed no significant improvement after a prolonged course of glutamic acid therapy. Much better results, however, were obtained in the group with dystrophy. These patients received glutamic acid daily (10 Gm.) in milk. They are classified as follows: (1) a man who had suffered from pseudohypertrophic muscular dystrophy for twenty-three years and who after ten weeks of treatment with glutamic acid, glycine and ephedrine began to gain weight, exhibited a more stable gait and experienced better muscular control generally; (2) a woman who had suffered from functional atrophy of the legs subsequent to a protracted period of rest in bed and who made a substantially complete recovery following a few weeks of glutamic acid therapy, and (3) a man who had suffered for twenty-one years from progressive muscular dystrophy and showed marked improvement after one month of treatment with glutamic acid; his wobbling gait disappeared, he was able to walk miles without fatigue and he gained markedly in weight.

Reviewing the literature, the authors point out that in patients with muscular dystrophy improvement has generally been reported following therapy with amino-acids. Pseudohypertrophic muscular dystrophy, myasthenia gravis and progressive muscular dystrophy, in particular, are improved by the administration of glycine or glutamic acid. On the other hand, patients with atrophy suffering primarily from lesions of the spinal cord are little affected by treatment with amino-acids. They suggest that such therapy may have some value, however, in the acute and convalescent stages of infantile paralysis, by preserving the tone of the paralyzed muscles until regeneration of the affected nerves occurs. The biochemical explanation for the formation of creatinine from these amino-acids is demonstrated by chemical equations and structural formulas.

DAVIDSON, Newark, N. J. [ARCH. NEUROL. & PSYCHIAT.]

SCHÜLLER-CHRISTIAN DISEASE (XANTHOMATOSIS): REPORT OF A CASE WITH POSTMORTEM OBSERVATIONS. J. M. WHEELER, Arch. Ophth. **11**:214 (Jan.) 1934.

In 1930 Wheeler reported a case in which he demonstrated that the exophthalmos in these cases is due to xanthomatous nodules in the orbit. He now records another case in which a careful examination was made during the child's stay in the hospital, followed by a complete report of the postmortem observations.

WESCOTT, Chicago.

PNEUMOCOCCAL LIPOID NEPHROSIS AND THE RELATION BETWEEN NEPHROSIS AND NEPHRITIS: I. CLINICAL AND ANATOMICAL STUDIES. S. S. BLACKMAN JR., Bull. Johns Hopkins Hosp. **55**:1 (July) 1934.

This is a study of the etiology, pathogenesis and nature of lipoid nephrosis. Clinical and anatomic data from ten cases of nephrosis in children are given. The experimental work on the effect of pneumococcus toxin on the tissues of animals will be described in a subsequent paper.

Blackman finds no evidence that lipoid nephrosis is a metabolic disease, diabetes albuminurinicus. Clinical and pathologic data are presented which point to the etiologic relation between chronic pneumococcic infection and the pathogenesis of some examples of lipoid nephrosis. He believes that it is a particular form of diffuse nephritis and that microscopic hematuria and slight elevation of the blood pressure may occur at times. From data collected he believes that the edema of nephrosis cannot be explained by mechanical factors alone, and that there is good evidence that widespread capillary damage is one important factor in the pathogenesis of edema in nephrosis.

Every one will not agree with Blackman's interpretation of various findings, but the clinical and anatomic material is excellent and very complete.

LYTTLE, New York.

MASTITIS ADOLESCENTIUM. A. E. HARBESON, Canad. M. A. J. **30**:648 (June) 1934.

A tumor in the breast of a 10 year old girl is reported. The tumor was in the upper outer quadrant of the left breast; it was about 3.5 cm in diameter, slightly movable, easily defined, not adherent to the skin and fairly hard on palpation. It increased in size somewhat, and a swelling appeared in a month. Later a similar condition developed in the right breast.

Harbeson's conclusions are:

1. Mastitis adolescentium is a condition seen in girls at puberty and is caused by mechanical obstruction of the lactiferous ducts.

2. It is a result of unbalance between the follicular and luteal hormones which bring on mammary development at adolescence.

3. The condition does not predispose to malignancy.

MOORE, Omaha.

ENDOCRINE DWARFISM. W. ENGELBACH and R. L. SCHAEFER, Endocrinology **18**: 387 (May-June) 1934.

This is a second report following further the course of seven patients whose preliminary response to treatment was recorded in a previous paper. All were grossly undersized, and their clinical histories over a protracted period of time suggested a practically stationary growth. All had been treated with thyroid by mouth without showing any stimulation of growth. During periods of from three to five months' treatment with a commercial preparation containing the growth hormone of pituitary (antuitrin-G) the increase in height varied from 1 to 2 7/10 inches (2.54 to 6.9 cm.).

Patients 1 and 2 discontinued treatment because after several months more of injections no further satisfactory growth increment was noted. Patient 1 showed a normal osseous development. In patient 2, a girl, aged 15 years, the administration of the growth hormone resulted in the production of amenorrhea on two occasions. These reactions illustrate the previously expressed views of the authors, namely, that in the presence of normal sexual development and function or of normal or advanced osseous development therapy with this hormonic substance is of little or no value. This is explained by a supposed antagonism between the sex and growth factors elaborated by the anterior lobe of the pituitary gland. Patient 6, who had grown 2 7/10 inches during five months of treatment, refused to cooperate further. Four patients who continued treatment with growth hormone (to which thyroid was added in three instances) increased from 3.3 to 6 inches (8.4

to 15.24 cm.) in height in fifteen months. In all four of these cases there was definite retardation in osseous development varying from one to four years. A significant roentgenographic finding of fuzzy, ragged, poorly outlined appearance of the osseous centers and epiphyses, together with decreased density of bone, is described in nine of the fifteen cases of this type which have come under the observation of the authors.

The recommended dosage of growth hormone is 2 cc. two or three times a week, and it is believed that thyroid therapy to tolerance is a valuable adjunct.

JACOBSEN, Buffalo.

FAMILIAL INFANTILISM DUE TO HYPOPHYSEAL AND THYROID INSUFFICIENCY. J. C. M. FOURNIER, R. A. L. HELGUERA, C. A. CASTIGLIONI and B. ANIDO, Endocrinology **18**:533 (July-Aug.) 1934.

An interesting family, a brother and four sisters, suffering from infantilism due chiefly to hypophyseal insufficiency is reported on. The outstanding clinical features were reduction in the size of the body, atrophy of the sex organs in the male, absence of menstruation in the females, a low basal metabolic rate and excessive sensitivity to cold, delayed epiphyseal closure and absence of mental retardation. The etiology of this disorder cannot be charged to insufficiency of the thyroid gland, because there had been no retardation in the age of learning to walk and talk, and there was no marked mental retardation. Therefore, the primary cause is considered to be hypophyseal imbalance with secondary involvement of the thyroid.

After a course of thyroid treatment in three of the patients the basal metabolic rate was increased and sensitivity to cold lessened.

JACOBSEN, Buffalo.

ASTHMA IN CHILDREN. R. A. COOKE, J. A. M. A. **102**:664 (March 3) 1934.

The incidence of asthma in children has been roughly estimated at 2.5 per thousand of population. The importance is not in its great frequency or high mortality but essentially in the fact that in those afflicted with it the morbidity is high; thus this means that in children, aside from the economic aspect, it interferes with nutrition, education and recreation. Asthma is now defined as a dyspneic state caused by an allergic reaction involving the bronchi and bronchioles. The allergy may be immediate—that is, the asthma may develop almost immediately after contact with the substance—or it may be delayed for two to three days. In the latter case skin tests with the specific substance give uniformly negative results, and immune bodies are not demonstrable in the serum. These delayed allergies are responsible for some of the unsatisfactory results of tests. Heredity plays a most important part in the etiology of asthma. The substances exciting the asthmatic attacks may be inhaled from the air, ingested as foods or drugs, injected subcutaneously or absorbed from foci of infection which are usually located in the upper respiratory tract.

Treatment of the acute attack consists in hypodermic administration of epinephrine in sufficient amounts. When the attack is severe, codeine or morphine may be necessary. Oxygen is used for cyanosis. Ipecac in doses large enough to produce vomiting may be very useful. In the milder cases ephedrine with amytal is useful. Most important is the treatment directed toward the actual cause. Accurate and complete diagnosis of all the causes is the essential of successful treatment. Specific treatment of the skin-sensitive type is avoidance of the cause. Infants usually outgrow the sensitiveness, but in older children in whom this is not the case injection of specific allergens must be resorted to. In treatment of the infective type, early eradication of the infection in the pharynx and nasopharynx is indicated. The failure of tonsillectomy the author believes is due to deferring the operation too long or to faulty operative technic. Roentgen treatment of infected sinuses in children under 15 years of age seems to be effective. The effect of vaccine therapy is difficult to evaluate. The treatment with autogenous vaccines that produce symptomatic asthma gives the best results.

Nonspecific measures as a whole are unsatisfactory. So far as preventive treatment is concerned, there is no known way to prevent the development of a predetermined allergy of the immediate type to foods or air-borne substances. Manifestation of an instinctive dislike for certain foods is of practical value. For predisposed children unnecessary animal contacts are undesirable, even before symptoms develop. When the predisposed child shows a tendency to frequent "colds," early and complete removal of the tonsils and adenoids is indicated, in the mind of the author. In all cases treatment should be begun with the first indication of an asthmatic tendency, for proper control of these early attacks reduces the incidence of a return of the trouble. BONAR, Salt Lake City.

RESEMBLANCE OF CERTAIN TUMORS OF THE HYPOPHYSIS TO TUMORS OF THE JAW. E. B. Fink, J. Am. Dent. A. **21**:997 (June) 1934.

Attention is called to the resemblance of certain tumors of the hypophysis to those found in the jaw. Particular note is made of adamantinomas and odontomas. Tumors of both regions frequently occur in young persons. Two cases are reported.

NOYES, Chicago.

THE RELATION OF SERUM PROTEIN FRACTIONS TO SERUM SICKNESS IN RABBITS. L. JONES and M. S. FLEISHER, J. Immunol. **26**:455 (June) 1934.

In a previous communication the authors showed that symptoms of serum sickness may be produced in rabbits by the injection of a foreign serum. In this paper the ability of the different protein fractions to produce serum sickness is reported. Euglobulin, pseudoglobulin and albumin were obtained from horse serum by precipitation of the fractions with ammonium sulphate.

Pseudoglobulin was the fraction largely responsible for the production of serum sickness. Euglobulin was effective only when injected in large amounts, and albumin had essentially no effect. The combination of either of these two fractions with pseudoglobulin did not appear to influence the occurrence of serum sickness.

The authors suggest the possibility that these results may be due either to some other substance precipitated with the pseudoglobulin or to some variation in the configuration of pseudoglobulin in individual serums.

FOTHERGILL, Boston.

ETIOLOGY OF GRANULOPENIA (AGRANULOCYTOSIS). ROY KRACKE and FRANCIS P. PARKER, J. Lab. & Clin. Med. **19**:799 (May) 1934.

Kracke and Parker express the opinion that a large percentage of cases of agranulocytosis are the result of the oxidation products of certain commonly used drugs which contain the benzamine group, namely, benzine, acetanilid, phenacetine, amidopyrine and arsphenamine. They found in their studies that agranulocytosis is more prevalent among those persons who would be more likely to use these newer synthetic preparations. There are still, however, a certain number of cases which cannot be explained on this basis. MCMURRAY, Galveston, Texas.

VERRUCOUS AORTITIS WITH SPECIAL REGARD TO ANEURYSM FORMATION IN CHILDREN. BENJAMIN H. NEIMAN, J. Lab. & Clin. Med. **19**:929 (June) 1934.

Reports of three instances of involvement of the aorta following rheumatic fever are given. All three patients showed one common feature, that is, verrucous aortitis. The verrucae are formed as a result of fibrinoid swelling and necrosis of the intima. Rupture and aneurysm result from necrosis that destroys the internal elastic membrane, with subsequent weakening of the media.

MCMURRAY, Galveston, Texas.

Symptoms Suggestive of Duodenal Ulcer Arising from Hookworm Infection. J. Heyward Gibbes, J. South Carolina M. A. **30**:102 (May) 1934.

Gibbes reports several interesting cases of infestation with hookworm suggestive of duodenal ulcer and differentiated only by careful analyses. He concludes that the symptoms caused by parasitic infection in the duodenum include a hunger pain without the clocklike regularity of that in true ulcer. The pain is frequently located in the left upper part of the abdomen, and there is no intermission as in cases of a true ulcer. Persons with parasitic infections in the duodenum do not have the typical symptoms of ulcer. Eosinophilia is present in hookworm infection. Examination of the stools reveals the eggs of Uncinaria. The roentgen rays will not differentiate ulcer from the parasitic infestation.

Weston Jr., Columbia, S. C.

Allergy in Children. M. Murray Peshkin, M. Rec. **139**:536 (May 16) 1934.

The procedure employed in a search for the etiologic symptoms of an allergy involves the taking of a history carefully and in detail, protein tests, a thorough physical examination and the use of laboratory and other diagnostic aids when necessary. Peshkin discusses the various tests briefly, and, in more detail, eczema, pollen allergy and asthma. Change of environment may bring about entire relief from the symptoms. Change of climate should be recommended to those patients who have undergone a careful investigation and in whom allergic and other treatment proved unsuccessful. It should be borne in mind that patients are spoken of as being relieved and not cured in allergic disease. The predisposition to the condition always remains with the patient. Much progress has been made in this branch of medicine within the last twelve years, and still further research will remove many difficulties which are encountered at present.

Williamson, New Orleans.

Notes on Giant-Cell Tumors of Bone and Cysts. Frederic J. Cotton, New England J. Med. **210**:1095 (May 24) 1934.

The typical giant cell tumor occurs in the shaft end (not epiphyses) of the tibia or femur at the knee, of the humerus high up, or of the radius at the wrist, while cysts, at least those of the "solitary cyst" type, occur farther from the ends of bones. In practice either may occur anywhere. In this series are cases of giant cell tumors of the jaw, of the scaphoid of the foot, of a metatarsal, two cases of tumors of the phalanges of the hand, two of tumor of a metacarpal, one of tumor of a patella and one of probable vertebral involvement. Cysts in this series occurred in or close to the head of the femur in four cases, close to the knee in one, close to the tibial head in three, at the ankle in one, close to the shoulder in two, in a metacarpal in one and in the pelvis in one. On the other hand, eight were cysts in the shaft. So the line is far from sharp.

Reasons for refusing to have an open operation are fear of a biopsy, which is surely not logical in the face of a diagnosis of giant cell tumor, and fear of infection, which does not seem to occur with adequate technic. Operation, as a rule, brings about real repair of the tumor, as well as of the milder cases of cyst.

Gengenbach, Denver.

Diaphragmatic Hernia: Medical and Surgical Treatment. S. Allen Wilkinson, New England J. Med. **210**:1105 (May 24) 1934.

This report is concerned chiefly with the medical handling of the smaller varieties of diaphragmatic hernia and a discussion of the symptomatology arising from its presence. Before the advent of roentgenography hernia of the abdominal organs through the diaphragm was recognized chiefly at the autopsy table and was thought to be a comparatively rare condition occurring only after severe crushing injuries or from congenital defects in the diaphragm. With the increasing fre-

quency of roentgen examinations it is now generally accepted that diaphragmatic hernia is by no means infrequent.

The cases summarized here illustrate the fact that only a small number of such hernias required surgical intervention or caused the death of the patient, while most of them were readily amenable to treatment and a few caused no symptoms of any kind.

Associated gastro-intestinal complications are common and may produce the only symptoms of which the patient complains. Successful medical treatment must be directed against the associated conditions rather than the hernia itself in nearly all instances. Surgical treatment should be reserved for those cases in which medical treatment fails to control the symptoms. Phrenicotomy is advised as a preliminary to more extensive procedures, and it alone may relieve the condition.

GENGENBACH, Denver.

A CASE OF HYPERINSULINISM WITHOUT DEMONSTRABLE PANCREATIC CHANGES IN AN ELEVEN YEAR OLD CHILD. JOHN A. BOONE, New England J. Med. **211**:49 (July 12) 1934.

The disease is characterized by a consistently low blood sugar, with resulting symptoms of hunger, weakness, nervousness, tremors, sweating, trembling, mental lapses and, in severe cases, unconsciousness and convulsions. A number of patients with hyperinsulinism have been operated on or have come to autopsy, with the discovery of adenomas consisting of pancreatic islet cells or of carcinomas with the same histologic basis. In cases in which operative removal of the tumor was possible, complete and lasting relief from symptoms and a rise of the blood sugar to normal levels were obtained.

After prolonged observation in the hospital this patient was operated on, but no pathologic change was found in the adrenals, liver or pancreas. The patient made an uneventful recovery and was discharged and put on frequent feedings of low carbohydrate content, as recommended by Seale Harris. The specimen of pancreas removed at operation showed an abundance of islets and one very large islet, but no definitely diagnostic abnormality.

GENGENBACH, Denver.

THE ABDOMINAL TRINITY IN INFANTS AND YOUNG CHILDREN. R. M. STEPHENSON, New Orleans M. & S. J. **86**:731 (May) 1934.

Stephenson cites numbers of cases of gastroduodenal ulcer in very young patients, these ulcers having been diagnosed on operation or at autopsy. The patients ranged in age from 10 days to 10 years. Cases of chronic ulcerated cholecystitis and cholelithiasis in young children are also reported. An able review of the literature on disease of the gallbladder in children is included. The difficulty of diagnosing appendicitis in young children is stressed; the author states that very early perforation or gangrene often disguises the picture. The criteria of the diagnosis of appendical disease are carefully outlined so that the triad of pediatric abdominal disease looms on the diagnostic horizons.

SMITH-FINE, Dallas, Texas.

SOME EXPERIMENTAL OBSERVATIONS BEARING ON THE ETIOLOGY OF MEGACOLON. HAROLD BURROWS, Brit. J. Surg. **21**:577 (April) 1934.

In these experiments powdered crystalline silica was introduced into the mesentery of the cecum, and a fortnight later intraperitoneal injections of 1:2:5:6—dibenzanthracene were given once a week in doses of 1 cc. of a 0.1 per cent solution of the hydrocarbon in emulsified olive oil. In the eleven rats given the injections there was enlargement of the cecum. Burrows explains these results by the chronic irritating effect of the silica on the sympathetic nerves which produced the megacolon.

SUMMERFELDT, Toronto, Canada.

ASCARIS LUMBRICOIDES IN THE PERITONEAL CAVITY. P. K. RAO, Half-Yearly J. Mysore Univ. **7**:1, 1933.

Ascaris lumbricoides was found in the peritoneal cavity of a child. Some of the ascarids were dead and buried on the surface of the liver, intestine and spleen, and others were living and free in the peritoneal cavity. Intestinal perforation was not seen at the postmortem examination.

FROM THE AUTHOR'S SUMMARY [ARCH. PATH.]

AN INVESTIGATION INTO THE CLINICAL VALUES OF THE LEVULOSE AND GALACTOSE TOLERANCE TESTS FOR HEPATIC FUNCTION, M. V. RODHAKRISHNA RAO, Indian J. M. Research **21**:141 (July) 1933.

The levulose tolerance reaction was positive in some but not all cases of disease of the liver. It was normal in some cases of cirrhosis in which there had been regeneration. The galactose tolerance reaction was found too variable to be relied on absolutely.

SNELLING, Toronto, Canada.

IS HALOMETRY RELIABLE? A STATISTICAL VIEW. H. P. CHAUDHURI, Indian J. M. Research **21**:315 (Oct.) 1933.

The author carried out Price-Jones measurements and halometer readings on a number of blood smears. He found that there was practically no difference between the average size of the cells by either measurement.

SNELLING, Toronto, Canada.

STUDIES ON INFANTILE BILIARY CIRRHOSIS: III. OBSERVATIONS ON INFANTILE BILIARY CIRRHOSIS IN VIZAGAPATAM. M. V. R. RAO, Indian J. Pediat. **1**:166 (April) 1934.

Rao's observations on infantile biliary cirrhosis show that the incidence of disease in Vizagapatam is greatly exaggerated, and that it is practically limited to Hindu children of the middle and rich classes between the ages of 1 and 2 years. The diet of the children affected with the disease differed in no way from that of normal children of the same age class. Although cases of enlargement of the liver due to dietetic irregularities are commonly seen in the poor class of children, typical manifestations of infantile biliary cirrhosis are not seen in them, even if the condition is neglected or untreated. The clinical features of the three stages of the disease are described. The pathologic picture in the liver is that of a peculiar type of intracellular cirrhosis with proliferation of bile ducts. The diagnosis, differential diagnosis, prognosis and treatment are briefly described, and some of the important theories about the causation discussed.

GONCE, Madison, Wis.

ACROMEGALY IN ONE OF UNIOVULAR TWINS. AUBREY LEWIS, J. Neurol. & Psychopath. **15**:1 (July) 1934.

A pair of uniovular twins 46 years old are reported who were almost identical in appearance and size until the age of 14. Thereafter one began to grow faster and was soon taller and stronger than his brother. At present A. is 6 feet, 4 inches (193.04 cm.) tall, while his twin brother's height is 5 feet, 8 inches (172.72 cm.). The acromegaloid giant sustained an injury to the head at the age of 12, and while the literature does not credit cranial trauma with causing acromegaly, a few instances may be found in which this anomaly of growth may be traced to the injury, as evidenced by pathologic changes in the sella turcica observed at autopsy. Lewis thinks that while the predisposition to gigantism is undoubtedly inherited, there may be a relationship between the cranial trauma which this patient sustained and the acromegaly.

JAHR, Omaha.

DIABETES MELLITUS IN CHILDREN. LESLIE COLE, Lancet **1**:947 (May 5) 1934.

This paper is based on observations on eighteen patients with diabetes mellitus who at the time of onset were less than 15 years old. They attended Addenbrooke's Hospital in Cambridge for supervision, as a rule not oftener than once every two months, as the great majority lived from 10 to 50 miles (16.1 to 80.5 kilometers) distant.

The age at onset varied considerably. The earliest onset was at 3 years. The disease was familial in six patients, but evidence of heredity could be traced in only one of these.

Of the infectious diseases mumps was an immediate prelude to the onset of the symptoms of severe diabetes in three cases. Mild infections preceded the onset of symptoms in three cases, but in the remainder the diabetes appeared to have come on silently.

None of the cases could be called mild.

On admission to hospital the patients were usually placed on a diet containing from one third to one half of the caloric requirements for their age, the carbohydrate not exceeding 40 Gm. In most patients a small dose of insulin was given from the beginning and gradually increased until the twenty-four hour specimen of urine was free from sugar and the blood sugar within normal limits (a matter of from one to four weeks). The patients were kept in hospital from one to two months. In the severe cases of long duration it was not found possible to increase the carbohydrate above 110 Gm. In the milder cases it was found that the diet could be varied considerably on the same dose of insulin without any corresponding change being observed in the blood sugar readings or urinalyses. No hard and fast rule was followed as to either the total number of calories given or the relative proportions of the different elements.

Every severe exacerbation in a patient with established diabetes was associated with some infection. An acute infection was nearly always the cause of diabetic coma.

"In some patients in whom control is difficult the choice lies between a very strict regime with rather curtailed activities and a normal blood sugar and no glycosuria; and a normal life with a fuller diet, a raised blood sugar, and frequent glycosuria." In such a case Cole considers the latter course preferable.

Diabetic coma occurred six times in four patients. Acute empyema of the antrum developed in one patient. The two patients who died were moribund on admission.

So far as growth and development were concerned, these patients compared favorably with other children of the same age and class. In intelligence they seemed rather above the average. Their activity was not restricted in any way.

LANGMANN, New York.

HYDATID DISEASE OF THE LUNG. R. G. PROSSER EVANS, Lancet **1**:1281 (June 16) 1934.

An average of three patients with hydatid disease are admitted to the Swansea Hospital each year. Human infection is usually due to eating unboiled vegetables soiled by the excreta of dogs or contaminated by flies. The commonest site of the disease is in the liver; the next most frequent location is in the lung, in the ratio of about 10:1.

Evans reports a case in an 8 year old girl who on first examination showed dulness and coarse crepitations over the right lung. She was seen irregularly in the course of the next two years. Roentgenograms showed a fairly dense shadow involving a large part of the right lung. Two Pirquet reactions were negative. On three occasions she had violent bouts of coughing and coughed up "pieces of skin" in addition to much foul sputum. She was admitted to the hospital, and the expectorated material was identified as the wall of a hydatid cyst, but no hooklets were found. The child was treated symptomatically and was discharged much improved.

Evans states that "with reservations, the dictum of Trousseau must still be accepted—viz.: 'Generally speaking, the wisest course is to refrain from interference and be the watchful observer of nature's method.'"

LANGMANN, New York.

OBSERVATIONS ON HEMOCHROMATOSIS. K. MADDOX and E. B. DURIE, M. J. Australia **1**:463 (April 7) 1934.

Maddox and Durie describe the clinical and biochemical findings in four cases of hemochromatosis. Their summary and conclusions are as follows:

"1. Suggestions are made as to the natural history of the disease, which include the hypothesis of selective toxic damage to the liver, affecting the ability of the liver cells to store and release iron, related metals and glycogen.

"2. Since cirrhosis and pigmentation of the liver are the only features common to all cases, we are of the opinion that hemochromatosis is merely a syndrome of liver cirrhosis in general and not a separate disease entity. It represents an advanced state of 'pigment cirrhosis.'

"3. The disturbance of carbohydrate metabolism is partly pancreatic, but mainly hepatic, wherein the extent of iron deposition is a fairly accurate index of the degree of interference with glycogenlysis and glycogenesis, possibly due to deficient formation of insulin kinase. In the few patients benefited by insulin, damage or dysfunction of the pancreatic islets is assumed to be present.

"4. Prolonged epigastric pain is of evil prognostic omen.

"5. We consider that further work in this field can be best applied in the direction of ascertaining the character of the iron and copper balance over an adequate period and by close biochemical investigation of the terminal coma of the disease, which clinically has points of difference from both true diabetic coma and cholaemia, together with further research on the glycogen and pigment metabolism in other types of liver cirrhosis."

GONCE, Madison, Wis.

CIRRHOSIS OF THE LIVER AND SPLENOMEGALY IN THREE BROTHERS. FREDERICK LANGMEAD, Proc. Roy. Soc. Med. **27**:939 (May) 1934.

The brothers affected were aged 13, 11 and 9 years, respectively. The eldest boy in the family, aged 16, and another brother, 12 years old, were healthy and well. The only complaint of the last two patients was hematemesis of a few months' duration. The results of physical examination and of examinations of the blood and urine, as well as of the hepatic tests, are given in full. Splenectomy was performed in one case, and the pathologist's report on sections of spleen is also given.

WILLIAMSON, New Orleans.

ACHOLURIC FAMILY JAUNDICE IN AN INFANT. ROBERT HUTCHINSON, Proc. Roy. Soc. Med. **27**:942 (May) 1934.

The patient was an infant of 4½ months and the youngest of five children. The first and third children had had their spleens removed on account of acholuric jaundice. The history of the patient, with results of examination of the blood, made every few days, is given.

WILLIAMSON, New Orleans.

HEPATOMEGALIA GLYCOGENICA WITH INFANTILISM IN TWO SISTERS. HUGH THURSFIELD, Proc. Roy. Soc. Med. **27**:943 (May) 1934.

This condition occurred in two sisters, aged 14 and 12 years, respectively. The family history and patients' history and the results of physical examination and biochemical investigations are given fully in the report, which is accompanied by a photograph of the patients.

WILLIAMSON, New Orleans.

DISCUSSION ON THE ETIOLOGY OF ACUTE RHEUMATISM AND CHOREA IN RELATION TO SOCIAL AND ENVIRONMENTAL FACTORS. Proc. Roy. Soc. Med. **27**:953 (May) 1934.

The discussion was opened by J. Alison Glover. He refers first to the report of the Child Life Committee of the Medical Research Council on "Social Conditions and Acute Rheumatism," which appeared in January 1927. He then takes up the degree of poverty which causes the highest incidence, the etiologic significance of infection, institutional epidemics and familial infection.

Other members taking part in the discussion were Reginald Miller, W. S. C. Copeman, E. C. Warner, R. J. Llewellyn, Bruce Perry, J. A. Nixon, Fortescue Fox, Leonard Findlay, E. W. Goodall and Gray Hill.

WILLIAMSON, New Orleans.

RECOVERY OF SIGHT AND HEALTH IN A CASE OF GIGANTISM. E. A. SEALE, South African M. J. **8**:371 (May 26) 1934.

Seale reports the sudden recovery of sight and health in a 10 year old greatly overgrown boy who had been showing signs of increased intracranial pressure for three years and failing vision for six months. GONCE, Madison, Wis.

POSTURAL DRAINAGE IN THE TREATMENT OF ACUTE PYELITIS. V. VERMOOTEN, South African M. J. **8**:405 (June 9) 1934.

Postural drainage in the treatment of acute pyelitis suggested by Vermooten is based on the fact that (1) excursion of the kidneys for several centimeters takes place with each respiration and (2) the downward movement of the kidney is responsible for the so-called ureteral kink, which under normal conditions is only a slight degree of tortuosity. When acute pyelitis exists "the tissues of the pelvis and probably of the upper part of the ureter, become edematous and infiltrated with inflammatory products so that they become inelastic. The tortuosity of this inelastic ureter during inspiration or when the patient is in the upright position then becomes an actual angulation or 'kink,' and thus acts as a partial or complete obstruction to the free egress of fluid from the renal pelvis." By raising the foot of the bed from 6 to 12 inches (15.24 to 30.48 cm.) and allowing the patient only one small pillow under the head, the kidney will tend to stay in a high normal position, thereby keeping the ureter straight and promoting better drainage. Application of this idea aided by the intake of bountiful amounts of fluid resulted in marked shortening of the febrile period of acute pyelitis and seemed to aid the urinary tract in overcoming the infection.

GONCE, Madison, Wis.

CHRONIC CERVICAL ADENOPATHY IN A CHILD OF FIVE YEARS. P. NOBÉCOURT, Ann. d'anat. path. **10**:416 (April) 1933.

This child had a massive swelling on the left side of the neck, which had first appeared when she was 2 years of age. Residence at the seaside for a year was without benefit. No positive result was seen from nine skin tests and four intradermal tests. Biopsy showed the condition to be reticulosis resembling lymphogranulomatosis, but without Sternberg cells. Roentgen therapy was administered from October 12 to December 7 as follows: 2,500 roentgens in five sittings over the thorax in front, 2,500 in five sittings over the thorax behind and 4,000 in eight sittings to the neck. Treatment was interrupted by an attack of measles. When the patient returned to the clinic on December 24 the tumor had disappeared, and no further treatment was given. In the succeeding March she was in good health, and biopsy showed only the usual lesions of adenitis. The swelling seems to have been a lymphogranuloma not to be classified as of the variety Paltauf-Sternberg.

VINTON, Brooklyn.

OCULAR DISORDERS IN GAUCHER'S DISEASE AND NIEMANN-PICK'S DISEASE. NORDMANN, Ann. d'ocul. **171**:445 (May) 1934.

Nordmann reports that Gaucher's disease in infants is differentiated from the classic form in adults by the prominence of nervous symptoms. In Gaucher's disease in adults clinical examination of the eye always gives negative results. Motility is often disturbed in infants affected with Gaucher's disease.

BERENS, New York. [ARCH. NEUROL. & PSYCHIAT.]

ABDOMINAL PAIN IN CHILDREN. A. LÜÜS, Arch. de méd. d. enf. **37**:345 (June) 1934.

Among children between the ages of 3 and 8 years abdominal pain is found in two distinct groups: those in whom other symptoms of disease exist, as in pleurisy, pneumonia, disorders of the liver, kidney and bladder, and those children who are not ill in the general sense of the term but who complain of recurrent pain of greater or less duration and at irregular intervals. Often these attacks are intensely severe; the patient shrinks, becomes pale and utters piercing cries, while clasping the region of the umbilicus. The onset is not connected with the ingestion of food, and Lüüs maintains that in most cases the condition occurs in the colder months.

Friedjung described this syndrome in 1902 and considered it a manifestation of the infantile type of hysteria; Moro, in 1913, classified this recurrent umbilical colic as the psychogenic factor of a neuropathic constitution. In the first group, appendicular colic, chronic in its course and due to foreign bodies, including intestinal parasites, seems to be a common variety, while adhesions and displacement of the appendix, abnormal mobility of the cecum, inflammation of Meckel's diverticulum, epigastric hernia and transient invaginations of the bowel are regarded among the rarer etiologic factors. Tuberculosis of the mesenteric glands is a common source of abdominal pain, as is also helminthiasis. Ylppo has called attention to the frequency of gastroptosis and gastrectasia, with hypo-acidity, in children between the ages of 7 and 12 years. Renal calculus and abnormal mobility of the kidney are among the unusual sources of acute ventral pain in early life, while biliary calculus is reported by Kellog to have been found in but sixty-four instances in two hundred years.

In the management of the patient in whom the condition is psychogenic, simple removal to the hospital brings prompt cessation of the pain in certain instances; in others, suggestion, faradization or hot packs are employed.

AMESSE, Denver.

PARALYSIS IN THE COURSE OF HELMINTHIASIS: REPORT OF A CASE. S. SALAZAR DE SOUZA, Arch. de méd. d. enf. **37**:479 (Aug.) 1934.

Calamida and Massinedo produced convulsions and paralysis experimentally in dogs with extracts of Taenia. It is asserted that such results are due to an intoxication of the elements of the central nervous system. De Souza reports a case of a boy of 11 who complained for three months of increasing difficulty in walking. Examination revealed absence of reflexes in the legs without loss of sensation and with no trophic disturbance; there was no paresthesia, and the eyegrounds were normal. In the absence of the parents, an adequate history could not be obtained. The Wassermann reaction of the spinal fluid was negative, but in spite of this a tentative diagnosis of juvenile tabes was made. At this point De Souza was advised by an attendant that several years previously the boy had passed some segments of a tapeworm. An anthelmintic was administered, and five days later a large specimen of Taenia saginata was expelled. Improvement began at once, and complete restoration of function was reported after several weeks. The patient was assiduously followed for more than a year and continued to be in excellent health.

AMESSE, Denver.

SCHÜLLER-CHRISTIAN DISEASE. A. BOSQUET, Gaz. méd. de France, p. 110, Feb. 1, 1934.

This disease occurs in boys three times as often as in girls. It is characterized by osteoporotic lacunae, especially in the skull; unilateral or bilateral exophthalmos; diabetes insipidus, and arrest of growth. The lacunae are most abundant in the cranial vault; they vary in size from that of a pea to that of the palm of a large hand; they have a scooped-out appearance, but some are funnel-shaped and others involve only one table. The base of the cranium may be affected. In 30 per cent of cases the sella turcica is either enlarged, deepened or eroded or its surface is destroyed. The bones of the face may show disappearance of the outline of the orbit or excavation of the inferior maxillary bone, the teeth having no hard foundation and tending to fall out. Often the pelvis is implicated, particularly the ilia, which are frequently deformed. There is sometimes involvement of the upper end of the diaphysis of the femur, of the humerus, the ribs, scapulae or vertebrae. In some cases there are nodular growths of bones, roughening, obscuring of the sphenoid sinus and excrescences of the skull and iliac bones. The disease tends to self-cure, but may result in death from cachexia. Roentgenotherapy is the only treatment, causing disappearance of the peripituitary xanthomatous masses and so influencing diabetes and growth.

VINTON, Brooklyn.

MEGADUODENUM IN AN EIGHT YEAR OLD HEREDOSYPHILITIC BOY; SUCCESSFUL GASTRO-ENTEROSTOMY. F. BÉRARD, JAMIN and THOMAS, Lyon chir. **30**:182 (March-April) 1933.

Two successive roentgenographic examinations showed a stomach at first atonic and later hyperkinetic, opening into a second well defined pouch. This pouch occupied the place of the second portion of the duodenum, being evenly and proportionately dilated and containing liquid and extending downward almost to the right iliac fossa. It bore a close resemblance to a second stomach, undergoing violent contractions. The barium sulphate meal passed regularly but with difficulty into the upper part of the jejunum. The stomach and the dilated duodenum emptied very slowly. A roentgenogram taken eighteen hours after ingestion of the barium sulphate meal showed the barium sulphate still in the lower portion of the small intestine and the ascending tract of the large intestine. At operation the upper part of the jejunum was found to be obstructed by a congenital band connecting it with the root of the mesentery.

VINTON, Brooklyn.

CONGENITAL MALIGNANT TUMORS OF THE LIMBS. PIERRE LOMBARD and LE GENISSEL, Rev. d'orthop. **21**:297 (July) 1934.

Congenital malignant tumors of the limbs are extremely rare. The authors report a case of a cavernous angioma occurring in an infant and present at birth. The left forearm appeared grossly enlarged. Treatment with radiation was given, which controlled any increase in size of the tumor. One year later the tumor was removed at operation. The tumor lay in the soft tissues without any bony attachment. Amputation was advised, but permission for this was refused. The child died four months later. Histologic examination of the tumor showed the mass to be similar to a fusiform cell sarcoma, mitotic figures being numerous.

RYAN, Vancouver, Canada.

DETERMINATION OF p_H IN THE DIFFERENTIATION BETWEEN EXUDATES AND TRANSUDATES. G. C. DOGLIOTTI and T. TODOROW, Boll. d. Soc. ital. di biol. sper. **8**:1765, 1933.

It is possible to distinguish exudates from transudates by determining the ratio of blood p_H: liquid p_H. In the exudates the ratio is unity or greater than unity (from 1 to 1.04); in the transudates it is less than unity (from 0.967 to 0.998).

KUGELMASS, New York.

CHOLESTEROL GRANULOMATOUS LIPOIDOSIS. C. NATALI, Pediatria **42**:861 (July 1) 1934.

A case of cholesterol granulomatous lipoidosis in a child 3½ years of age which terminated in death is reported. Natali presents a full discussion of the classification of this type among other lipoidoses, together with a consideration of the clinical and pathologic characteristics.

SIGNORELLI, New Orleans.

TWO CASES OF MALIGNANT GRANULOMA. E. PEZZA, Pediatria **42**:981 (Aug. 1) 1934.

This paper represents a report of two cases of malignant granuloma, together with the author's research in the literature and some clinicostatistical considerations concerning the etiology, symptomatology and therapy of this condition.

SIGNORELLI, New Orleans.

PULMONARY ABSCESS PROBABLY OF AMEBIC ORIGIN CURED WITH EMETINE HYDROCHLORIDE. E. A. BERETERVIDE and PEDRO ALURRALDE, Arch. argent. de pediat. **5**:6 (Jan.) 1934.

This rare complication occurred in a boy 12 years old. A prominent symptom was severe pain over the right shoulder blade, which was particularly aggravated on percussion. Both percussion and auscultation indicated the presence of pulmonary consolidation in the lower lobe of the right lung.

There was moderate fever, which finally dropped to normal, with persistence, however, of all the pulmonary signs.

An exacerbation of all the symptoms and recurrence of high fever and hemoptysis led the authors to suspect amebic infection after tuberculosis and syphilis had been ruled out. The condition responded remarkably rapidly to the use of emetine hydrochloride and remained completely cured.

SCHLUTZ, Chicago.

HYDROLABILITY IN EARLY INFANCY. SALVADOR E. BURGHI, Arch. argent. de pediat. **5**:63 (Feb.) 1934.

Certain infections, particularly latent otitis media and diphtheritic renal inflammation, chronic digestive disturbances, prolonged hypo-alimentation, both qualitative and quantitative, and certain types of acidosis can so profoundly alter the histologic structure and the functional capacity of the cellular tissue that it becomes incapable of fixing fluids. This condition occurs more readily in an organism which constitutionally seems inclined to this dysfunction.

SCHLUTZ, Chicago.

SUBACUTE ENDOCARDITIS. JOSÉ M. MACERA and JUAN C. OYHENART, Arch. argent. de pediat. **5**:82 (Feb.) 1934.

The authors report a case of this condition in a child 10 years old in which the symptoms continued for over a year. There were marked cardiovascular changes. Prolonged attacks of fever alternated with afebrile periods. Erythema nodosum and urticarial eruptions appeared periodically. Marked anemia developed, but moderate leukocytosis was almost constantly present. Blood cultures never were positive. The patient eventually recovered.

SCHLUTZ, Chicago.

BLUE SCLERAS AND FRAGILITAS OSSEUM. J. CASANOVAS, Arch. de oftal. hispano-am. **34**:133 (March) 1934.

After a brief review of the literature on the relations between blue scleras and fragilitas osseum and of the theories presented on its causation and on the influence of heredity, Casanovas reports a case in a boy 9 months old with no

hereditary antecedents and with four brothers in whom no such condition was found. This child was born at term after normal labor. He was fed first on condensed milk, then on cow's milk and finally on a farinaceous milk food. He was poorly nourished. The scleras were very blue, and the bones of the cranium excessively thin, with open communicating fontanels. There was clinical and roentgen evidence of consolidated fractures as follows: in the right clavicle, in four ribs on the right side and two on the left, in the two humeri (double on the right side), in the left ulna and radius, in the two femurs (double on the left side) and in the left tibia.

The child died of a gastro-intestinal disorder, and an anatomopathologic examination of both eyes was made. This showed only excessively thin scleras and marked uveal pigmentation, to which circumstances the blue color of the scleras can be attributed.

FINLAY, Havana, Cuba. [ARCH. PATH.]

CONGENITAL PYLORIC STENOSIS. MARTINHO DA ROCHA, Arch. de pediat., Rio de Janeiro **5**:227 (April) 1933.

Da Rocha believes that surgical intervention is the treatment for pyloric stenosis. He gives a general review of the subject and reports several of his own cases.

HERRON, Spokane, Wash.

HEMOPTYSIS IN PULMONARY DISEASES OF CHILDHOOD. LUIS MORQUIO, Arch. de pediat. d. Uruguay **4**:466 (Nov.) 1933.

In the experience of this distinguished clinician, pulmonary hemoptysis is practically always associated with the condition of hydatid cyst in the lung. He has, however, observed the condition with increasing frequency in pulmonary tuberculosis. It can occur in cases of nontuberculous pulmonary inflammation. He reports two such cases in which tuberculosis, hydatid cyst and dyscrasia of the blood were ruled out and yet severe hemorrhage from the lungs was present.

SCHLUTZ, Chicago.

PERINEPHRITIS IN THE INFANT. CARLOS GIANELLI, Arch. de pediat. d. Uruguay **5**:108 (March) 1934.

Gianelli reports this condition in two infants—one 2 months and the other 8 months old. Both infants had cutaneous staphylococcic infections. Following slight gastro-intestinal disturbances, a focus of perirenal infection developed in the right lumbar region in the younger infant and in the left lumbar region in the older infant. At operation large collections of pus were found in the perirenal region in both cases. Both patients made an uneventful recovery.

SCHLUTZ, Chicago.

A PECULIAR CLINICAL CASE. CLODOVEU DE OLIVEIRA, Movimento pediat. **1**:65 (April) 1934.

When the child was first observed he had a gastro-intestinal disturbance. Bronchopneumonia resulted, and it was finally determined that he had congenital syphilis.

SANFORD, Chicago.

PATHOGENESIS OF INFANTILISM AND ITS RELATIONSHIP TO THE GLANDS OF INTERNAL SECRETION. SANTIAGO CAVENGT, Pediatría españ. **23**:1 (Jan.) 1934.

Infantilism is not an independent disorder, but is rather the resultant syndrome of a combination of various diseases operating in a predisposed organism. It is not congenital and is not an arrested development, as many authors believe. It represents evolution which has lost its normal growth rhythm, which has been replaced by retarded or aberrant growth. The syndrome has its beginning in

infancy. The author has coined the term pathocavitism, meaning that there are disturbances of growth and that the children inherently are frail and weak.

In the pathogenesis of pathocativism, various etiologic factors must be considered: (1) a direct cause located, for example, in the endocrine glands; (2) a predisposed tissue; (3) exogenous factors in the nature of infection or a nutrition factor, which may precipitate manifestations of disease.

Pathocativism may be uniglandular or pluriglandular. These forms can be subdivided into somatic and psychosomatic types, depending on whether the changes are simply morphogenetic or are combined with psychic retardation. These forms or types can again be subdivided into hypotrophic and dwarfed types.

SCHLUTZ, Chicago.

CLINICAL PICTURE OF SPLENIC ENLARGEMENT. R. ARMAS CRUZ, Rev. chilena de pediat. **62**:166 (March) 1934.

The author discusses in detail various conditions associated with splenic enlargement. Operative removal of the spleen is advised in primary splenic anemias and also in syphilitic anemias, if they are resistant to all forms of medical treatment. The outcome of the operation is more favorable if the procedure is undertaken in the early or secondary stages of these disorders. The operation is contraindicated if the anemia is pronounced and the number of red blood cells is below 1,000,000. A tendency to thrombosis is present on account of the likelihood of mesenteric thrombosis.

SCHLUTZ, Chicago.

MANAGEMENT OF ENURESIS. JOSEF SIEGL and HANS ASPERGER, Arch. f. Kinderh. **102**:88 (May 25) 1934.

This article consists of a discussion of the treatment of enuresis in seventy-six cases managed according to Hamburger's methods. Suggestion is the basis of the treatment. After organic disease is ruled out the parents and child are told confidently that the enuresis can be stopped. Complete confidence in the physician is essential. The power of suggestion is reenforced by medication, faradization, high frequency current or hospitalization when needed. Seventy-two per cent of the children were completely and permanently cured of enuresis, and the remainder were greatly benefited. Several illustrative histories of cases are reported in detail.

LEMASTER, Evanston, Ill.

CHLORIDE EXCRETION IN ACUTE HEPATITIS IN CHILDHOOD. G. TÖRÖK and L. NEUFELD, Arch. f. Kinderh. **102**:102 (May 25) 1934.

In nine cases of acute hepatitis in children the amount of sodium chloride excreted in the urine was quantitatively the same as in normal children receiving the same intake of sodium chloride. Even in cases of severe damage to the liver the amount of sodium chloride in the urine was dependent on the intake, just as in well children. Török and Neufeld conclude that in children the amount of sodium chloride excreted is of no value in testing the liver function.

LEMASTER, Evanston, Ill.

PATHOGENESIS OF ADIPOSOGENITAL DYSTROPHY. R. M. MAISLISCH, Arch. f. Psychiat. **99**:35, 1933.

There is a review of the literature in the first section of the article. Most authors believe the disturbance to be one of dysfunction of the pituitary gland.

Maislisch investigated the effect of various extracts of glands of internal secretion on the excretion of urine, the urinary chloride and the basal metabolism of patients with this condition. These patients show diabetes insipidus. After pituitary was given the excretion of water decreased, the chloride increased and basal metabolism was little changed. Epinephrine caused the excretion of urine to rise,

while the chloride increased, and the basal metabolism was raised. When pituitary and epinephrine were given together the urinary secretion decreased. Salyrgan decreased the excretion of urine, increased the excretion of chlorides and increased the basal metabolism markedly. When pituitary and salyrgan were given together the effect of the salyrgan was increased. Thyroid extract had little effect except to raise the basal metabolic rate. Prolan also had little effect. Maislisch concludes from his work that the disturbance is not one of the pituitary body alone but rather of all the glands of internal secretion. He found that the diuretic salyrgan had the opposite effect in these cases. SNELLING, Toronto, Canada.

EFFECT OF THYROXINE ON THE THYMUS. HANNA SCHULZE, Beitr. z. path. Anat. u. z. allg. Path. **92**:329, 1934.

To determine the interrelations of the thyroid and thymus, new-born white mice were given daily subcutaneous injections of thyroxine, beginning on the day after birth. The effect on the thymus was determined at varying periods after birth. There was an absolute as well as a relative decrease in the size of the thymus. When the injections of thyroxine were not begun until the thirteenth day of life thymic atrophy was less marked. In comparable experiments on new-born white mice, rabbits and kittens the two last-named species were found to be less resistant to the toxic action of thyroxine, and a lesser degree of atrophy of the thymus resulted. The simultaneous injection of thyroxine and an extract of the thymus enhanced the toxic action of thyroxine.

SCHULTZ, Evanston, Ill. [ARCH. PATH.]

CORRELATION OF THE ANTERIOR LOBE OF THE HYPOPHYSIS AND THE CORTEX OF THE ADRENALS. HEINTZ KALK, Deutsche med. Wchnschr. **60**:893 (Jan. 15) 1934.

Kalk describes a typical case of hypophyseal cachexia or Simmonds' disease in a 14 year old boy. The symptoms were: loss of weight; poor appetite; hypoglycemia; hypersensitiveness to insulin; low basal metabolism (to minus 35 per cent); hypotension, with a systolic pressure of 95 and a diastolic pressure of 75; a pulse rate of 60 per minute, and psychic changes consisting of lack of cooperation, bad manners, hysteria and infantile behavior. There were signs of hypofunction of the secretion of the pancreas, as shown by a considerable amount of neutral fat and undigested muscle fibers in the stool.

The patient was treated first for twelve weeks with extract of the anterior lobe of the hypophysis given perorally and parenterally, without improvement. However, when 60 Gm. of adrenal extract was administered subcutaneously, improvement set in within three days. The medication was continued for twelve weeks, during which time all the symptoms disappeared. Improvement continued even after the cessation of the treatment. There was a period during the treatment when the basal metabolism became positive and the patient became slightly hypertrichotic, had a rapid pulse rate and complained of easy fatigability. However, these symptoms disappeared when adrenal therapy was discontinued.

The author knows of one other case of Simmonds' disease reported in the literature in which adrenal therapy was successful. KERESZTEERI, New York.

RUDIMENTARY FORMS OF RELAXATIO DIAPHRAGMATIS. M. VENSCHOTT, Monatschr. f. Kinderh. **59**:432, 1934.

Venschott suggests that the name "relaxatio" be applied to all conditions in which the diaphragm stands unusually high. Such a condition results only from injury to a muscle or nerve. In nine hundred and eighty-five roentgen examinations he found twenty cases of rudimentary types of this condition in which one side was only slightly higher than the other. These are associated with distention of the stomach with air. The latter is not a cause but a result. There is no

physiologic relaxatio in childhood. Children with low diaphragmatic tone may present such a picture if the stomach is distended artificially, but the duration is only temporary. Rudimentary relaxatio, like the more definite forms, is evidence of injury to the phrenic nerve, usually from pressure of large hilus glands. The most frequent factor is, of course, tuberculosis, though whooping cough and other diseases may play a rôle.

GERSTLEY, Chicago.

PNEUMOCOCCUS PROBLEMS IN CHILDHOOD. GERHARDT JOPPICH, Monatschr. f. Kinderh. **60**:205, 1934.

In a study of seventy-eight children pneumococci were typed from smears from the throat cultures of sputum and organisms obtained from the secretions in complications. Sixteen of the patients had lobar pneumonia. The organisms in lobar pneumonia and its complications were of the fixed types I and II. The organisms obtained in bronchopneumonia as well as its grave complications belonged to type X. The mortality of infection due to the X type is, of course, much the highest.

GERSTLEY, Chicago.

HELMINTHIASIS IN CHILDHOOD (1932-1933). H. BRÜNING, Monatschr. f. Kinderh. **60**:224, 1934.

Brüning reviews the literature on this subject of 1932-1933, including the last months of 1931. Ascaris is most frequent. Using the method of Zschucke (4 Gm. of stool plus 56 cc. of one-tenth solution of sodium carbonate made homogeneous in a flask) and counting the eggs in one drop in a pipet for blood-counting, it was found that the average content of ascaris eggs was 6,700 per gram of stool in twenty-two children, as against 1,580 oxyuris eggs per gram of stool in eleven children. Efforts are still being made to make a diagnosis through skin reactions and, recently, through determining the speed of absorption of intracutaneously injected solution of sodium chloride. Absorption is supposedly quicker in the infected children.

Eosinophilia was absent in one series of three hundred and twenty-five children, but was present in other series. Parasites are evidently much more common in Europe than in this country. Swiss statistics show an incidence of from 22 to 38 per cent; French, from 36 to 51 per cent, and Chinese, up to 80 per cent.

The clinical symptoms are open to discussion. Some statistics suggest that infections lead to disturbance of growth and intelligence. Others cannot confirm this. Some reports suggest a relation of infection to allergy and state that infected children are subject to pleuritis, eczema, asthma and bronchial infection. The surgical complications are usually those of intestinal obstruction and sometimes abscess formation. Nothing new is offered in medication.

GERSTLEY, Chicago.

TREATMENT OF SPONTANEOUS PNEUMOTHORAX. E. SCHOTT, München. med. Wchnschr. **81**:716 (May 11) 1934.

Schott reports a case of spontaneous unilateral pneumothorax in a man aged 42 years, which did not respond to rest, repeated aspiration or the intrapleural injection of 30 per cent dextrose solution. After seven months 0.5 cc. of oil of turpentine was injected intrapleurally. The patient complained of severe pain and went into shock (pleural shock), which responded to treatment. The pleural exudate was gradually absorbed, and the lung expanded.

BRAHDY, Mount Vernon, N. Y.

DIFFERENCES IN BLOOD PRESSURE IN THE UPPER AND LOWER EXTREMITIES. A. EDELMANN and A. KAHAN, Wien. Arch. f. inn. Med. **24**:377 (Feb.) 1934.

Differences in the blood pressure in the upper and lower extremities depend on hindrances which may arise in the course of the blood stream and may lead

to loss of kinetic energy. The rectangular branching off of the artery of the arm is significant in the development of these differences. Syphilitic changes of the aorta which lead to a distortion and narrowing at the point of origin of the vessels of the arm raise the differences in the blood pressure through increased resistance.

The so-called Hill symptom is of practical significance. In doubtful cases it would cause one to suspect the existence of syphilitic disease in the upper part of the aorta. Arteriosclerotic changes which lead to narrowing of the lumen of the vessel can decrease pressure in the artery and so lead to a difference in pressure.

SCHLUTZ, Chicago.

EFFECT OF INSULIN ON THE ACETONE BODIES. A. LÖW and A. KRČMA, Wien. Arch. f. inn. Med. **24**:455 (Feb.) 1934.

An increase in ketone bodies takes place in man as well as in the experimental animal about an hour after the injection of insulin. At the height of the effect of the insulin the augmentation of ketone bodies disappears and a diminution begins to take place. Glycogen deficiency in the liver plays a big rôle in the development of this phenomenon.

SCHLUTZ, Chicago.

A NEW CURATIVE PRINCIPLE IN EXUDATIVE ILLNESSES. OSKAR RIED, Wien. klin. Wchnschr. **46**:1001 (Aug. 11) 1933.

Ried reports the use of baths containing irradiated potassium salts in the treatment of exudative processes. The salts were treated with red rays and mercury vapor lamps. According to the author's experiments, no patients suffering from exudative illness remain indifferent to these baths. They were tried also in cases of tuberculous processes, and here, too, strong reactions were observed. The extent of the curative effects in cases of tuberculosis has not yet been determined. However, in diseases of the joints of widely different origin, which have not responded to previous treatment, the baths give good results in most cases, often cause extensive improvement and not infrequently lead to complete recovery.

ABT, Chicago.

TRICHINOSIS. M. I. LIPSHUTZ and M. O. BOKALCHUK, Vrach. delo **16**:813, 1933.

The authors present a detailed discussion on the etiology, pathology and symptomatology of trichinosis and describe in detail four cases of the disease. The outstanding features of the symptomatology in these cases were: (1) a sudden onset with a high fever of a remittent type and chills, (2) general malaise, (3) edema of the face and eyelids, (4) profuse perspiration and (5) muscular pain and tenderness of a variable degree.

The authors believe that the severity of the symptoms and the prognosis depend on the amount of the ingested trichinae, and a small amount may thus be ingested without demonstrable symptoms. The edema of the eyelids and the eosinophilia are considered by the authors to be the most constant and characteristic findings of trichinosis.

As to the prophylaxis, the authors recommend outside of the general public sanitary measures, cooking of pork at a temperature of 80 C. (176 F.), which is the temperature at which the color of the meat is changed from red to gray. Salting and smoking processes are insufficient to destroy the parasites, unless salting is accomplished with very strongly concentrated solutions.

BODER, Chicago.

SUGAR THRESHOLD AND KIDNEY FUNCTION. T. BJERING and P. IVERSEN, Acta med. Scandinav. **82**:193 and 228 (May 24) 1934.

The authors determined the plasma and urinary creatinine and the plasma and urinary sugar every ten minutes after the ingestion of 4.5 Gm. of creatinine, then of dextrose in doses of 5 Gm. in 130 cc. of water every five minutes.

Creatinine and dextrose pass into the glomerulofiltrate in the same concentration in which they are present in the capillaries of the glomeruli. While it is not reabsorbed through the tubuli, the dextrose or a part of it is reabsorbed.

From the data the authors calculate the concentration of dextrose of the reabsorbed fluid. If there is no glycosuria during the test, the reabsorbed fluid necessarily must have a higher concentration of dextrose than the plasma. If glycosuria develops the concentration of the reabsorbed fluid must drop below the plasma level (the threshold for rising blood sugar), and when the glucosuria ceases it rises again above the blood sugar level (the threshold for falling blood sugar). The first threshold is higher.

The sugar content of the urine depends on: (*a*) the blood sugar level and (*b*) the concentration of the reabsorbed fluid. If diuresis is great the second factor is negligible.

KAJDI, Baltimore.

THE SIGNIFICANCE OF OVARIAN HORMONE PREPARATION FOR MALES. S. E. DE JONGH, Nederl. tijdschr. v. geneesk. **78**:1208 (March 17) 1934.

In males an ovarian hormone preparation is known to have the following effects: 1. An antimasculine effect (in noncastrated males). Whether the quantity of estrogenic substance in males has any significance in this respect is questionable. The antimasculine effect obtained by therapeutically administered female sex hormone is reversible.

2. Paradoxical effects in castrated males (growth of tissues in so-called male organs) as follows: (*A*) An analog of the thickening of the walls of the fallopian tubes, uterus and vagina in females is the thickening of the smooth muscle and connective tissue layer of the seminal vesicles and ducti deferentes (with a pacemaker effect for the specific action of male hormone based on such development of the walls of these organs). (*B*) An analog of the proliferation of stratified epithelium in females is the proliferation of artificially produced stratified epithelium close to the opening of the ducts of the seminal vesicles and prostate, while a number of points of similarity to hypertrophy of the prostate are significant. These effects are counteracted by male hormone. Favorable effects of male hormone in light cases of hypertrophy of the prostate in man have been noted.

The question is asked whether the estrogenic substance extracted from male organs and body fluids is identical with "ordinary" ovarian hormone preparation ($C_{18}H_{22}O_2$ as a ketone).

VAN CREVELD, Amsterdam, The Netherlands.

Nervous Diseases

FAMILIAL FACIAL PARALYSIS. FRANK VAN DER BOGERT, Arch. Pediat. **51**:262 (April) 1934.

A case of facial paralysis occurring in an infant of 6 weeks is reported. This palsy, which was unilateral and confined to the lower area of the face, was present from birth, and a similar condition was discovered in the child's father and in the father's cousin.

WADDELL JR., University, Va.

THE RELATION BETWEEN HANDEDNESS AND SOME PHYSICAL AND MENTAL FACTORS. ARTHUR B. FITT and K. H. O'HALLORAN, J. Educ. Psychol. **25**: 286 (April) 1934.

Fitt and O'Halloran conclude from observations among primary and secondary grade school children that there is a definite correlation between handedness and scholastic ability, left-handedness being associated with low scholastic ability. Furthermore, in a group of children of the average age of from 12 to 13 years, the data indicated that those dominantly left-handed showed more psychopathic tendencies than those dominantly right-handed. Left-handed boys of from 13 to 14 years were somewhat shorter than right-handed boys, with a tendency to reversal at 15 years and an equally slight tendency to physical dominance of right-handed boys at 16 years of age.

ABRAMSON, New York.

THE PATHOGENESIS OF NARCOLEPSY. M. LEVIN, J. Neurol. & Psychopath. **14**:1 (July) 1933.

Narcolepsy is defined as the condition in which transitory paralysis with tonelessness, occurring in response to sudden emotion, is associated with morbid sleepiness. In more than two hundred cases of narcolepsy reported in the literature, there are described sixteen cases of sleep paralysis, i. e., a paralysis, local or general, occurring either while the patient is falling asleep or while he is awakening therefrom. The pathogenesis in these cases is explained on the basis of Pavlov's explanation of sleep as an irradiation of inhibition from localized areas of the cortex, which, in the alert animal, is a normal occurrence to the entire brain simultaneously. Cataplexy and sleep paralysis represent a dissociation of inhibition, a "localized sleep,'" in which the motor centers are inhibited while the substrate of consciousness is still active. Illustrative of the reverse condition is the performance of complex motor acts automatically in sleep, such as walking and talking.

The dispersion of cataplexy and sleep paralysis by extraneous stimuli, such as touch; the occurrence of powerlessness in consequence of the effort to ward off sleep or without apparent cause; the occurrence of hallucinations during sleep paralysis; the occurrence of postdormitial paralysis after fear dreams, and the occurrence of sleep attacks as a reaction to pain that must be borne without flinching, phenomena that have been frequently reported in narcolepsy, find a fitting explanation within the folds of this conditioned reflexology.

SPERLING, Philadelphia. [ARCH. NEUROL. & PSYCHIAT.]

MEGALENCEPHALY. S. A. KINNIER WILSON, J. Neurol. & Psycopath. **14**:193 (Jan.) 1934.

The subject of megalencephaly was chosen as the presidential address before the Section of Neurology of the Royal Society of Medicine in October 1933. This term is restricted to normal appearing, well proportioned enlargement of the brain and its parts. The literature is surveyed to ascertain the normal limits of the weight of the brain in relation to age, sex, race, cranial capacity, body weight and size and to different social and intellectual classes. Well known attempts to associate abnormal weights with mental endowment are reviewed. Two personal cases of megalencephaly in children are reported. The distinctive histologic feature in one case was a generalized dysplasia of the ganglion cells, chiefly of the third and fifth cortical layers, consisting "in a flattening or lateral shrinkage and elongation of the cytoplasm of many, its homogeneous coloration and the absence of Nissl granules, and also in a similar oval lengthening of the nucleus, which itself stained very deeply and failed to disclose normal nuclear structure."

The relationship of the growth of the brain, particularly in acromegaly, to any secretion or condition of the endocrine glands has not been convincingly established. However, there is much accumulating evidence to suggest that a neurohormonal mechanism may be responsible for growth changes in the nervous system. The well known neurohypophyseal and sympathetic adrenal medulla interrelationships and the demonstrations of chemical substances "secreted" by the terminals of nerve fibers, particularly of the autonomic nervous system, afford an adequate basis for such postulations. "If the brain contains within itself the apparatus whereby its own trophic growth is regulated, may we not conceive of the brain itself as a gland, its own gland?"

SPERLING, Philadelphia. [ARCH. NEUROL. & PSYCHIAT.]

CHRONAXIA OF EXPERIMENTAL POLIOMYELITIS. A. CHAUCHARD, B. CHAUCHARD, B. ERBER and P. MOLLARET, Ann. Inst. Pasteur **52**:444, 1934.

The latest model of the Lapicque apparatus, with a capacity of 90 volts and possible reduction to 1/200 of the voltage, was used on monkeys. The apparatus

appeared to measure adequately the neuromuscular excitability of the normal monkey. In order to prevent possible paralysis arising from injury to the brain, the authors resorted to intraperitoneal injections of the virus. There was a rigorous parallelism between the values of chronaxia and the evolution of paralysis. Since measurements indicated reaction before paralysis could be noted, during the period of incubation, a cerebral disturbance was indicated before infection was manifested, an infection which might become abortive or inapparent. In other words, "it demonstrates beyond doubt the constancy of a precocious encephalitic dissemination of the poliomyelitis virus until now unsuspected."

M. S. MARSHALL. [ARCH. PATH.]

PONTINE-CEREBELLAR ANGLE SYNDROME WITH SPONTANEOUS REMISSION. BREGMAN and LIPSZOWICZ, Rev. neurol. **1**:266 (Feb.) 1934.

A case of a tumor of the pons and cerebellar angle, with typical findings, is reported. There were found paralysis of the sixth nerve on the right, with convergent strabismus and diplopia; peripheral paralysis of the seventh nerve on the right; absence of the corneal reflex on the right, with a diminished reflex on the left; partial deafness on the right; nystagmus; difficulty in opening the mouth, and deviation of the tongue to the right. The symptoms developed progressively for six weeks, with no fever, headache or vertigo. There was vomiting during the first three weeks. Suddenly, while the patient was still in the hospital, the symptoms began to subside. The authors did not include in their report results of lumbar puncture or study of the blood serum, although they infer that all organic lesions of a syphilitic type were ruled out.

DAFFINEE, Boston.

LARYNGEAL PARALYSES FOLLOWING INJECTION OF THERAPEUTIC SERUM. H. ROGER, PRÉVOT, WAHL and BRÉMOND, Rev. d'oto-neuro-opht. **12**:419 (June) 1934.

Two cases of laryngeal paralysis following the injection of antitetanic serum are reported. In the first case the paralysis involved the dilator muscles of the glottis and the soft palate and appeared seven days after the injection; serum sickness developed and was followed within a few hours by the paralysis. Syphilis was definitely eliminated, and no cause other than the effect of the serum could be discovered. Nervous accidents following various forms of serum therapy are known. The paralyses are usually located in the brachial plexus but may be of the polyneuritic type; it is exceptional for the reaction to be localized in one or two cranial nerves. In this case the lesion is assumed to be in the bulbar nuclei of the tenth and eleventh nerves or their intrabulbar fibers. In the second case the right vocal cord and the aryteno-epiglottic muscle were involved, paralysis of the right superior and inferior laryngeal branches resulting. In spite of repeated and thorough examinations, no cause other than the serum sickness could be elicited. The only similar cases known to the authors are one reported by Lavrand and one reported by Schauwecker.

DENNIS, San Diego, Calif. [ARCH. NEUROL. & PSYCHIAT.]

PHOSPHORUS METABOLISM IN RELATION TO PATHOGENESIS OF SPASMOPHILIA. ALBERTO CABITTO, Pediatria **42**:838 (July 1) 1934.

Cabitto reports observations on the phosphorus metabolism of normal and spasmophilic children, with special reference to the action of guanidine in relation to phosphates on the isolated heart of the frog. He found that the addition of monosodic phosphate to Ringer's solution containing guanidine produces an increase of the positive inotropic and cronotropic action of guanidine.

SIGNORELLI, New Orleans.

TOXIC MOTOR APHASIA ASSOCIATED WITH PNEUMONIA. F. GROSSI and M. FAMIGLIETTI, Pediatria **42**:874 (July 1) 1934.

This paper represents the report of a case of pure toxic motor aphasia seen in a child 22 months of age on the second day after the onset of pneumonia, which persisted until three weeks after the crisis occurred. Complete recovery ensued.

SIGNORELLI, New Orleans.

PURULENT MENINGITIS WITH THE PICTURE OF TETANUS. MAMERTO ACUÑA and SAUL I. BETTINOTTI, Arch. argent. de pediat. **5**:1 (Jan.) 1934.

This rather rare form of purulent meningitis occurred in a child 8 months old. An exaggerated form of trismus was present and necessitated feeding entirely by nasal tube. The purulent spinal fluid showed the bacillus of Pfeiffer. Cisternal puncture and lavage and serum therapy gave no relief. At autopsy the entire brain was covered with purulent material.

SCHLUTZ, Chicago.

ACUTE PURULENT MENINGITIS IN THE INFANT. CARLOS GIANELLI, Arch. de pediat. d. Uruguay **5**:61 (Feb.) 1934.

Gianelli reports forty-one cases of this disorder, all occurring in infants under 2 years old. Thirty-five of the patients were under 1 year of age. In sixteen cases the condition was due to the pneumonococcus, in ten to the meningococcus, in ten to the Pfeiffer bacillus, and in one to the typhoid bacillus. In four the causative agent was not determined. The disease occurred more frequently in the spring than in the winter. The clinical picture was often confused with other common disorders of infancy. Lumbar puncture almost always establishes the diagnosis. The spinal fluid is always turbid, is practically always under tension and shows a high albumin content and polymorphonuclear leukocytosis. In meningococcic meningitis the author found the mortality to be 10 per cent. In this form of meningitis serum therapy is useful. It should be given by the spinal, intramuscular and subcutaneous routes. In one case it was given intraventricularly. In all other forms of meningitis the mortality was 100 per cent.

SCHLUTZ, Chicago.

A REPORT OF FOUR CASES OF SPASMOPHILIA WITH COMMENT. J. R. MARCOS and E. PELUFFO, Arch. de pediat. d. Uruguay **5**:102 (March) 1934.

Marcos and Peluffo believe that spasmophilia is a common disorder in Uruguay. It can occur in children in good nutrition. There is no obligate relationship to rickets. It occurs at the beginning of spring, independent of adequate light and sunshine. Convulsive seizures are common. Transitory infections precipitate the attacks. Erb's phenomenon is the most persistent sign of spasmophilia and the last one to disappear. The total blood calcium is generally somewhat lowered.

SCHLUTZ, Chicago.

CELLS OF THE CEREBROSPINAL FLUID. ALFRED BANNWARTH, Arch. f. Psychiat. **100**:533, 1933.

Bannwarth uses the method of Alzheimer, which consists in allowing the spinal fluid to drop into vital stain preparations at the time of puncture. The cells are stained while alive. By this method it is possible to tell whether the cells are inflammatory, degenerative or cast off from various parts of the brain. Bannwarth believes that the usual qualitative tests done on the spinal fluid are of little value.

SNELLING, Toronto, Canada.

FALSE INTERPRETATIONS IN ENCEPHALOGRAPHY. ELLI SAAMER, Monatschr. f. Kinderh. **59**:401, 1934.

Saamer reports studies on living children as well as on postmortem specimens. He shows several roentgenograms confirming his hypothesis, namely, that in performing encephalography the head must be held absolutely upright. In four of eight experiments on dead children and in two of six encephalographies on living children, he demonstrated that when the head is held in an abnormal position the air introduced does not diffuse uniformly throughout the subarachnoid spaces but tends to accumulate at the highest point.

GERSTLEY, Chicago.

THE NEISSER-POLLACK BRAIN PUNCTURE IN CHILDHOOD. P. VON KISS and I. FENYES, Monatschr. f. Kinderh. **59**:411, 1934.

The authors discuss the technic of this diagnostic procedure and give a diagram following the scheme of Kocher. This chart indicates the points on the skull through which a needle may be introduced to reach definite gyri of the brain.

The authors then describe a case in which they used such a diagnostic puncture and obtained fluid. The contents of the cyst indicated degeneration of a malignant tumor, which diagnosis was confirmed by operation.

GERSTLEY, CHICAGO.

ACUTE POLIOMYELITIS OF THE BRAIN STEM. P. VON KISS and B. HECHST, Monatschr. f. Kinderh. **59**:418, 1934.

This is an unnecessarily long, complicated clinical report of the case of a 7 year old boy dying of the pontile form of poliomyelitis. In both the clinical description and in the report of autopsy the authors emphasize the difficulty of making the differential diagnosis of this condition from epidemic encephalitis.

GERSTLEY, CHICAGO.

THE POLIOMYELITIS EPIDEMIC IN SZEGED, 1932. E. KRAMAR and I. LISZKA, Monatschr. f. Kinderh. **60**:136, 1934.

Kramar and Liszka report a series of ninety-nine cases. This epidemic was unusual in that 20 per cent of the patients were infants. Girls seemed much less susceptible than boys, showing much lower morbidity and mortality. Of the ninety-nine patients, sixty-six showed paralyses. Of the sixty-six, forty-five recovered in two months. Nine children died.

The clinical picture appeared in three types: (1) a catarrhal or gastrointestinal symptomatology without signs of involvement of the nervous system, (2) the same as 1, with mild meningeal symptoms and (3) outspoken meningeal symptoms.

The fact that thirty-three children were not paralyzed leads the authors to suggest that the disease may appear in two forms, paralytic and nonparalytic, and that the term abortive may be applied to either one of these if the condition is mild. In infants under 8 months of age the nonparalytic meningeal or nonparalytic abortive forms develop, with complete recovery. Infants over 8 months of age almost always are paralyzed and show a high mortality.

Six hundred and forty-seven examinations of the spinal fluid were made. If the globulin (Pandy) and fibrinogen (Waltner) reactions are negative or if the Pandy reaction is positive and the fibrinogen reaction negative, the prognosis is good. Should both be positive the prognosis is much more severe. The authors lay much emphasis on the mastic curve. Deviation from the normal is of grave significance. Fibrinogen disappears in the fluid rapidly, while globulin may remain for fifty days.

The treatment was large doses of adult serum. While this is by no means a specific, the authors believe that it is of value.

GERSTLEY, Chicago.

NERVOUS DISTURBANCES IN SCHOOL CHILDREN. JOSEF K. FRIEDJUNG, Wien. klin. Wchnschr. **46**:888 (July 14) 1933.

Friedjung states that school children between the ages of 6 and 14 years often show symptoms of nervousness for which poor training in the preschool years is usually responsible. The school period, however, causes these symptoms to take special forms. Especially for children who have never attended a kindergarten (the author is in favor of making kindergarten obligatory) the first day of school is a sensitive point in life. For neurotic children the beginning of school causes many difficulties of adaptation. Many fight against going to school or compensate for it at home by increased negativism. Others suffer from early wakefulness, trouble in dressing or at breakfast, vomiting at home, on the way to school or in school. On days when there is no school all these symptoms disappear; likewise, they disappear if the child is kept at home on account of them.

In the further course of school conflicts arise with the teacher or with fellow students. During the first four years the child is still bound to the family, and the teacher is merely another representative of the authority which the pupil feels in the home. According to his home experiences, the child sees in the teacher a good helper or a hard taskmaster. If the teacher is equal to his calling even neurotic children soon become adaptive. Beyond the age of 10 the problems become more complicated. Three periods may be distinguished: prepuberty, puberty and maturity. In girls the development is usually faster. In the first period comes a gradual breaking away from the parents. The critical faculty of the child is directed against the authority of the teacher; his inner life gains content, and friendships and the formation of groups become more marked. To children who develop rapidly and do not find much understanding at home the teacher becomes an all-important friend. Disturbances in neurotic children often lead to difficulties in learning. Sympathetic understanding and control are necessary. Sexual education must not exhaust itself in simple intellectual enlightenment, but must take hold of the child completely.

ABT, Chicago.

ENCEPHALOGRAPHY IN CHILDHOOD. KARL RUPILIUS, Wien. klin. Wchnschr. **47**: 587 (May 11) 1934.

Rupilius notes that the method of removing the cerebrospinal fluid and replacing it with a gas in order to obtain contrast in encephalography has proved most useful to neurologists and surgeons in the last ten years and has recently been applied extensively in pediatrics. The indications for encephalography are different and more comprehensive in children than in adults. While in adults the main indications are tumors of the brain, in children roentgenographic study should be undertaken in cases of chronic inflammation of the brain, epileptic convulsions and convulsions of unknown origin, congenital defects of the brain or defects caused by trauma at birth. In more than two hundred cases in which encephalograms were taken during the last ten years by the author there were usually defects in intelligence with various neurologic findings. It is emphasized that in order to interpret pathologic encephalograms normal pictures must be known in every detail. In 13 per cent of the cases a confirmation of the previous diagnosis was obtained with the encephalogram, and in 8 per cent of the cases the correct diagnosis was obtained only with this procedure. There were not many autopsies, but in sixteen cases in which an autopsy was performed the findings confirmed the roentgenographic results. As a contrast material the author used only air, introduced usually by lumbar puncture or, in the presence of special indications (e. g., hydrocephalus occlusus), by ventricular puncture. It is advantageous to make the investigation directly after the air has been introduced. In addition to the typical after-effects of lumbar puncture (headache, nausea, vomiting), the introduction of the air caused atypical results in the form of severe meningism in three cases, and in one case (one of the earlier ones) there was a fatality. The author has adopted the rule of introducing the air gradually and

takes care that more liquid is removed than air blown in. The chief value of encephalography is to confirm the clinical diagnosis, and in some cases the correct diagnosis is possible only by this procedure.

ABT, Chicago.

A SPECIAL FORM OF FAMILIAL MULTIPLE SCLEROSIS, RESEMBLING FRIEDREICH'S ATAXIA. B. BROUWER, Ztschr. f. d. ges. Neurol. u. Psychiat. **148**:321 (Nov.) 1933.

Brouwer reports the cases of two sisters with a characteristic picture of Friedreich's ataxia clinically; however, pathologic examination showed a number of disseminated plaques. The patients' father was addicted to the use of alcohol, and their mother suffered from hysteria. One brother and one sister died in infancy; both were idiots. Two other brothers and one sister were well. The disease began in both patients at 8 years of age, with disturbances in gait and tremors of the trunk and the extremities. The oldest sister had severe ataxia and tremors of the head and trunk; there was also ataxia of the legs. Sensation was not disturbed. The ocular fundi showed no atrophy. The upper abdominal reflexes were weak, and the lower abdominal reflexes were absent; there was a Babinski sign bilaterally. A diagnosis of Friedreich's disease was made. In the following years the ataxic disturbances increased markedly, and speech became much worse. Vision became worse because of atrophy of the optic nerves; nystagmus developed. The tongue was slightly atrophic, and the lower part of the right side of the face was slightly weak; swallowing was affected; hearing became impaired on the right; vertigo developed. The feet showed the characteristics typical of Friedreich's disease; the legs became very weak. All reflexes were lost, and there was a Babinski sign bilaterally. The condition remained constant, without remissions. A mild degree of dementia developed in the last few years of life. The patient died of a "grip" infection.

The younger sister was still alive at the age of 33. Her malady began at the age of 8, with disturbances in gait and tremor of the head. At the first examination there was mainly ataxia of the arms and legs; there was no intention tremor; the feet were in the equinovarus position. The reflexes were absent; the abdominal reflexes could be obtained. There was marked hypotonia of the extremities. At the time the case was reported there was almost complete inability to stand. There was no nystagmus, and speech was slow and monotonous. The legs were ataxic; the arms were dyssynergic. The tendon reflexes were absent, and the abdominal reflexes were decreased on the left. There were no Babinski sign and no sensory or mental disturbances. A diagnosis of Friedreich's ataxia was made. Later, mild atrophy of the optic nerves developed, and sensory signs appeared in the form of bilateral astereognosis and decreased muscle sense in all extremities; mental symptoms developed, with delusion and later deterioration; the ataxia reached a high grade. The disease progressed slowly; the optic nerves atrophied; horizontal nystagmus and ptosis developed; sense of vibration was lost in the legs. Serologic tests gave negative results.

Histologic study of the nervous system in the first case showed degeneration of the posterior columns and roots and the pyramidal tracts in the sacral part of the cord. At another sacral level there was a sclerotic plaque in the left anterior horn. In the lumbar and thoracic regions there was posterolateral sclerosis, the disease of the posterior columns spreading over to involve the posterior horns. The axis-cylinders remained intact. In the cervical region there were sclerosis of the posterior columns and circumscribed sclerotic patches. There were sclerotic plaques in the medulla, the nuclei of the posterior column, the left inferior cerebellar peduncle and the tuberculum acusticum, the pyramidal tracts, the reticular substance and the inferior olives. There were sclerotic patches in the cerebellum. Similar plaques were present in the walls of the third ventricle, the left internal capsule, the external geniculate body and the roof of the midbrain. Plaques were found in the cerebrum.

The clinical picture was that of Friedreich's disease; the pathologic changes were those of multiple sclerosis. There was no evidence of congenital syphilis, a similar picture having been described in congenital syphilis by Gianelli. Mondini described a case like Brouwer's. This concerned a woman, aged 32, with Friedreich's disease, who came of a family with marked mental degeneration. She died at the age of 41. Histologic study showed bilateral degeneration of the spinocerebellar tracts and slight demyelinization of the pyramidal tracts. There were atrophy and thinning of the cellular layer of the cerebellum. There were, in addition, sclerotic plaques in the cord and brain, with the classic characteristics of multiple sclerosis.

Brouwer believes that his patients suffered from a particular form of multiple sclerosis rather than from a special form of Friedreich's ataxia. The occurrence of disease of the pyramidal tract is more common in the former. Cases of the sort described are rare. ALPERS, Philadelphia. [ARCH. NEUROL. & PSYCHIAT.]

SYRINGOMYELIA IN TWO SISTERS, ONE OF THEM WITH A CEREBELLAR CYST. L. VAN BOGAERT, Ztschr. f. d. ges. Neurol. u. Psychiat. **149**:661 March) 1934.

There are about twenty reports of cases of familial syringomyelia, many of which are atypical. Van Bogaert records the occurrence of the disease in a family previously reported on by Verboogen and van der Vielde. The family history in these cases is bad. The maternal grandfather suffered from mental disease for many years. The mother was an alcohol addict and had cerebral arteriosclerosis. The father was an alcohol addict and died of delirium tremens. There were eleven children; four were healthy; four died of convulsions, typhus and tuberculosis, and three had syringomyelia. In one child this condition appeared at 8 years and in the other two at 12. Histologic study was carried out in one of the cases of syringomyelia, and typical cavities were present in the spinal cord.

The problem is whether syringomyelia occurring in families differs in any way from the sporadic disease. To answer this, van Bogaert reports two cases of his own. The patients were descended from a father who died of myocarditis and a mother who died of bronchopneumonia. There were two healthy children. In one of the cases there were signs of a cerebellar cyst. Autopsy revealed a cyst of the left lobus semilunaris, a cleft in the left side of the medulla and syringomyelic cavities in the cord. Histologic studies showed gliomatosis in the lumbar region and also in the cervical region of the cord. In the medulla there was a small slit, and in the cerebellum a cyst with smooth walls and without tumor; the cyst was surrounded by numerous sclerotic vessels. There was no ependymal epithelium anywhere in the cyst. There was no evidence anywhere of tumor formation. In the second case autopsy showed typical syringomyelic cavities in the spinal cord, most pronounced in the cervical region.

Van Bogaert asks whether these cases differ in any way from sporadic cases of syringomyelia; he concludes that they do not, either in the clinical or in the pathologic picture. The cerebellar cyst must be considered as being derived by cystic degeneration from a previous gliosis. The author suggests that some single cerebellar cysts may be of syringomyelic origin.

ALPERS, Philadelphia. [ARCH. NEUROL. & PSYCHIAT.]

ENCEPHALOGRAPHY AND THE EPINEPHRINE PROBE TEST FOR THE DIAGNOSIS OF TUMOR OF THE BRAIN. EICKENBUSCH, Ztschr. f. Hals-, Nasen- u. Ohrenh. **35**:533 (May 15) 1934.

Eickenbusch briefly describes and reproduces a roentgenogram for a case of glioma of the left occipital lobe. Neurologic examination in this case gave no evidence as to which side was affected. Only as a result of the epinephrine probe test of Muck was the localization established. The discovery of the ventricle on the normal side was easy, whereas the marked narrowing of the displaced ventricle would have made its localization on the involved side practically impossible. In

spite of the fact that he reports a single observation, the author believes that the practical value of the epinephrine probe test is demonstrated and that some of the complications of ventriculography may thus be avoided.

EDITOR'S ABSTRACT. [ARCH. OTOLARYNG.]

CONGENITAL PARTLY MALIGNANT NEOPLASM OF THE SCIATIC NERVE WITH CONSECUTIVE ELEPHANTIASIS. K. GROTH, Acta path. et microbol. Scandinav. **11**:44, 1934.

In a new-born boy the entire right sciatic nerve from the origin to the ends of the branches was the site of a mixed tumor of mesodermal origin. The tumor contained cartilage and was in parts sarcomatous. In the intradural part of the nerve were three nodules consisting of convoluted nerve fibers and fibromatous tissue. The case shows that primary tumors may develop in the peripheral nerves from the connective tissue of the nerve without the involvement of the sheath of Schwann. Broth reviews sixty-six recorded cases of congenital sarcoma and finds no previous instance of primary congenital sarcoma in the peripheral nervous system. The cause of the elephantiasis, which was predominantly lipomatous, appears to have been a disturbance of the circulation of the extremity due to pressure on the common iliac vein by the tumor. [ARCH. PATH.]

OCULAR CHANGES IN CASES OF JUVENILE AMAUROTIC IDIOCY. BENGT ROSENGREN, Upsala läkaref. förh. **3**:151 (Feb.) 1934.

Rosengren reports twenty-seven cases of Spielmeyer-Stock's disease which were studied clinically and pathologically. He states that the ocular changes present a uniform and practically always identical picture in both eyes of the same person. As a rule there is an acute onset between the ages of 5 and 8 years, with rapid loss of vision, leading to complete amaurosis in one year. During the early stages there is a granular appearance of the eyegrounds, especially of the macular region. The retinal vessels soon become narrowed, and the papilla becomes yellowish gray. Later, secondary pigmentation is to be seen in the papilla, which becomes pale. In the more advanced stages there is a greater increase in the amount of pigment, and frequently a posterior cortical cataract develops.

Anatomically, the disease is characterized, as Stock originally described it, by primary degeneration of the cones and rods followed by disintegration of the epithelial pigment cells. In the early stages no notable changes in the internal layers of the retina are to be seen. Later, however, there are pronounced changes, especially in the ganglion cells—changes identical with those in the cerebral ganglion cells. In the most advanced cases there is also atrophy of the optic nerve. Rosengren doubts the possibility of a uniform etiology for the degeneration of pigment. He thinks that there are probably a number of etiologic factors.

The rather large number of cases studied is due to the unusual organization for the care, supervision and study of blind children in Sweden.

NOTKIN, Poughkeepsie, N. Y. [ARCH. NEUROL. & PSYCHIAT.]

Diseases of the Eye

IRIDENCLEISIS IN BUPHTHALMOS. S. R. GIFFORD, Arch. Ophth. **11**:751 (May) 1934.

Because of the very unsatisfactory results obtained in most instances in cases of buphthalmos by various medical and surgical means, Gifford resorted to iridencleisis, with, in his opinion, a more satisfactory outcome. In his series of three cases with operation on five eyes he believes that three of the operations may be considered successful. He employed the Holth operation, but added the "watertight" conjunctival suture of Foster Moore. WESCOTT, Chicago.

OCULAR OBSERVATIONS AND STUDIES OF THE NEW-BORN, WITH A REVIEW OF THE LITERATURE. A. E. EDGERTON, Arch. Ophth. **11**:838 (May) 1934.

In this abridgment of a thesis submitted in a partial fulfilment of the requirements for graduate work in ophthalmology Edgerton reviews the literature of this subject and appends a lengthy bibliography. He examined the eyes of four hundred and fifty-eight infants shortly after birth. In his series, hemorrhage into the vitreous and anterior chamber was noted in two cases; nystagmus was found eighty-nine times, facial paralysis in two cases; opaque cornea, clearing in ten days; lenticular changes in one case; strabismus in eight cases; bilateral coloboma of the iris and choroid in one case, and pupillary membrane in twenty-seven infants. Blurring of the disks was seen in only six cases. Myopia was found in very few of the children.

Retinal hemorrhage was found in seventy-four boys, and in fifty-seven girls. Inequality of the pupils was found five times, and in four of these cases there was evidence of intra-ocular hemorrhage and intracranial pressure. Hemorrhage at the macula was found four times. The most common distribution of the hemorrhage was in the fibrous layer of the retina near the disk and along the vessels; small hemorrhages extended to the periphery.

With left occipital anterior presentation retinal hemorrhage occurred in the right eye twenty-eight times, in the left eye fifteen times and in each eye forty-one times. Retinal hemorrhage was found in the infant in fifty-eight of ninety-five low forceps deliveries, with bilateral hemorrhage occurring twenty-nine times. High forceps and midforceps deliveries were used seventeen times, with severe bilateral retinal hemorrhage in every case. Fifty per cent of the premature babies and 90 per cent of the immature babies showed retinal hemorrhage. Four immature babies delivered by cesarean section showed no hemorrhages, but three full-term infants delivered by cesarean section showed hemorrhages shortly after birth.

WESCOTT, Chicago.

IRIDOSCLERECTOMY IN INFANTILE GLAUCOMA: LATE RESULTS. PAUFIQUE, Bull. Soc. d'opht. de Paris, March 1934, p. 216.

A child 7 years of age was treated medically for a unilateral glaucoma for several months. The eye appeared to be increasing in size and was somewhat painful. The tension could not be obtained with an instrument because of the behavior of the child. A Lagrange iridosclerectomy was done under general anesthesia. Perception of light increased to ¼ after three years, and the tension remained normal. Paufique believes that in spite of poor vision and a bad prognosis in this type of case operation is indicated. MAYER, Chicago. [ARCH. OPHTH.]

TREATMENT OF PHLYCTENULAR CONJUNCTIVITIS. A. SCHWEITZER and A. OSORIO, Arch. Hosp. de niños, Roberto del Rio **4**:203 (Dec.) 1933.

Schweitzer and Osorio recommend treatment of the constitutional disposition by dietary measures, light and the use of phosphorized cod liver oil. For the photophobia and as a local measure to combat the pain and improve the ocular condition, they advise the use of strong protein silver, atropine and yellow mercuric oxide ointment. They place great reliance on the use of vaccine. They begin with doses of from 0.2 to 0.3 cc. of tuberculin. The maximum dose must not exceed 1 cc. The injections are given twice a week. No untoward reactions are observed with this form of treatment. Marked improvement or cure was noted in more than 70 per cent of their cases.

SCHLUTZ, Chicago.

INJECTIONS OF BLOOD IN THE TREATMENT OF PHLYCTENULAR DISEASES IN CHILDREN. KUNITOMO, Acta soc. ophth. jap. **38**:48 (June) 1934.

The mother's blood was injected intramuscularly into children with phlyctenular disease in which the symptoms of irritation were severe. At first 10 cc. was

injected, and subsequently from 10 to 2 cc. was injected twice a week. The symptoms of irritation were much improved, and the progress of the disease was shortened without complications. KNAPP, Chicago. [ARCH. OPHTH.]

Diseases of the Ear, Nose and Throat

ANOMALY OF THE INCUS-STAPES ARTICULATION AND OF THE STAPES. F. ALTMANN, Monatschr. f. Ohrenh. **68**:469 (April) 1934.

Altmann describes the case of a newly born child whose temporal bone showed chondrodystrophic changes. These changes have been described elsewhere. The tympanic cavities on both sides were of normal size and had normal lumens. The hammer had the usual shape bilaterally, as did the body and short process of the incus. The hammer-incus articulation showed no abnormalities. The long process of the incus was directly connected with the head of the corresponding section of the stapes without intervening articulation. This was present bilaterally. On the right side a connective tissue-bony connection existed by which the long process of the incus formed one continuous bony strand with the head of the stapes. On the left side there was a pure connective tissue binding between the two ossicles. The stapes was abnormally formed on both sides. On the right it was of normal size and formed a lamina; from the middle of the peduncle a stab-shaped process about as long as the peduncle arose; this extended into a headlike swelling above, while below it was slightly widened and bordered a small space. On the left a process rose from the nearly normally formed lamina which in its form and course appeared to represent the anterior pillar; above there existed a headlike enlargement.

In discussing this anomaly the author states that it can be best explained on a developmental basis, being most nearly paralleled by the developmental stage of an embryo of from 16 to 20 mm. Against the origin from chondrodystrophic changes is the absence of similar chondrodystrophic developmental anomalies in many cases of established chondrodystrophy.

EDITOR'S ABSTRACT. [ARCH. OTOLARYNG.]

THE FINER STRUCTURE OF THE TEMPORAL BONE IN CHONDRODYSTROPHY. F. ALTMANN, Monatschr. f. Ohrenh. **68**:539 (May) 1934.

Altmann describes the histopathologic appearance of the temporal bone in four cases of chondrodystrophy. The first was that of a 24 cm. long male fetus born spontaneously in the eighth month. The second was that of a newly born mature female infant. The third was that of a female infant born about two weeks before term, and the fourth was that of a new-born child of unknown sex. On the basis of the histologic observations the author agrees with Nager and Meyer that there are two types of changes in the temporal bone in chondrodystrophy. In the first there are slight changes, which consist solely of disturbances of the endochondral ossification and the corresponding low grade anomalies of the remaining primitive cartilage. In the second type, involving severe changes, marked disturbances of the endochondral ossification are found, with a partial substitution of ossification of the periosteal type richly filled with medullary cartilage. Marked anomalies of the primitive cartilage and partial replacement of this by strands of twisted bone tissue are also found. Naturally, however, the line between these two types is not sharply drawn. In regard to the origin and nature of the chondrodystrophic bone changes, the author is of the opinion that one is dealing with a developmental disturbance of the cartilage-forming system, presumably on the basis of an inferiority of the cartilage itself. The parallelism between the appearance of the cartilage and the degree of disturbance of ossification is corroboratory of this view.

EDITOR'S ABSTRACT. [ARCH. OTOLARYNG.]

CONSERVATIVE TREATMENT OF CHRONIC TONSILLITIS. G. E. JANNULIS, Monatschr. f. Ohrenh. **68**:612 (May) 1934.

Jannulis lays especial weight on the significance in the diagnosis of chronic tonsillitis of the objective sign of sensitiveness of the tonsillar niche to pressure obtained by palpation from outside. This sign can sometimes be made to disappear by employing conservative treatment instead of tonsillectomy. His conservative method involves massage and irrigation of the tonsillar crypts with methyl violet and collargol. The massage involves the buccinator, buccopharyngeal, glossopalatine, stylopharyngeal, glossopharyngeal, styloglossal, levator veli palatini, tensor veli palatini, pharyngopalatine, salpingopalatine and internal pterygoid muscles. In a patient with chronic tonsillitis whose case is described in detail the local symptoms and the general symptoms of lack of appetite, poor general condition and disturbed sleep were improved by this conservative method of treatment. The erythrocyte count increased from 3,600,000 to 4,600,000, and the percentage of neutrophilic leukocytes increased from 50.5 to 60.

EDITOR'S ABSTRACT. [ARCH. OTOLARYNG.]

FORMATION OF METASTASES IN OTOGENOUS PYEMIA DURING CHILDHOOD. I. HOFER, Monatschr. f. Ohrenh. **68**:713 (June) 1934.

Hofer reports the cases of two girls, each aged 7, who presented otogenous pyemia with the formation of pyogenic foci in the hip joint. He states that these metastases form more frequently in chronic than in acute cases of suppuration of the middle ear or disease of the sinuses. According to the experience of numerous authors, in chronic otitic processes mainly pulmonary metastases which have an unfavorable prognosis appear, while in acute diseases of the middle ear and sinuses the more benign and prognostically favorable metastases to the soft parts and joints predominate. Metastases of this origin rarely occur in the joints of children. When they do, they are found primarily in the large joints, such as those of the knee, shoulder, elbow and ankle. From a number of cases, the author cites only two in which the metastases were present in the hip joint. The complication was so serious in one case that it led to death. In the other, after repeated surgical intervention, a cure resulted, with partial ankylosis of the joint and shortening of the leg. If, in the course of otogenous pyemia, despite exclusion of the primary foci in the ear and in the blood vessels, pyemic manifestations such as fever and rigor persist, metastases must be the cause of the symptoms. If local pains are manifested, such as those due to abscess formation in the skin, muscles and joints, the diagnosis is easy. The presence of pulmonary metastases, abscesses and infarcts is confirmed by roentgen examination even if they offer few symptoms. The author particularly wishes to point out the grave prognosis of metastatic foci of suppuration in the hip joint, psoas muscle and true pelvis. The metastases must be treated surgically if conservative measures are not effective. Suppuration of the hip joint must always be treated surgically and not too late.

EDITOR'S ABSTRACT. [ARCH. OTOLARYNG.]

MEASUREMENTS OF SUBGLOTTIC PRESSURE IN CANNULA CARRIERS. W. BERGER, Ztschr. f. Laryng., Rhin., Otol. (Teil 1: Folio oto-laryng.) **25**:28, 1934.

In three patients on whom tracheotomy had been performed Berger measured the subglottic pressure under various conditions. The intratracheal cannula was attached to a T-shaped tube, one branch of which led to the manometer and the other to the writing point of the smoked drum. A water manometer was used except during pressure on the larynx or during coughing, at which time the pressure rose so high that a mercury manometer was necessary. In the first two patients the condition of the larynx approached normal; in the third patient cicatricial laryngeal stenosis was present. When the patients said the vowels a, o, u and e, slight increases in pressure occurred. When these vowels were whispered, the increase was much less. Pressure and coughing increased the sub-

glottic pressure markedly. The author states, however, that from the small number of patients examined no conclusions can be drawn as to the particular details of the function of the laryngeal muscles. A vocal range of less than two octaves must be of limited value. By the dynamometric method of observation, in which a rubber cylinder is introduced into the glottis, the sum of different forces (adduction force plus subglottic pressure) is measured. Dissociation analysis of these physical components is not, however, possible.

EDITOR'S ABSTRACT. [ARCH. OTOLARYNG.]

Diseases of the Skin

EPIDERMOMYCOSIS AT THE UNIVERSITY OF CALIFORNIA. ROBERT LEGGE, LEE BONAR and H. J. TEMPLETON, Arch. Dermat. & Syph. **29**:521 (April) 1934.

The authors report their results in the treatment of epidermomycosis with various preparations. The most favorable results were obtained with Whitfield's ointment to which 1.4 per cent thymol was added. The use of iodine gave the second highest per cent of satisfactory results as well as cures. Iodine possesses fungicidal activities in extremely high dilutions (from 1:100,000 to 1:250,000). They are hopeful in regard to iodine therapy for epidermomycosis. DULIN, Iowa City.

IODIZED TABLE SALT AS AN ETIOLOGIC FACTOR IN IODODERMA. PAUL E. BECHET, Arch. Dermat. & Syph. **29**:529 (April) 1934.

Bechet disapproves of the indiscriminate use of iodized salt over a long period without medical supervision. He believes that the use of the salt may sensitize the person to iodine and that its continued use or additional iodine given for medicinal purposes may produce ill effects from inveterate acne to severe iododerma. The histories of two patients with iododerma are given, both patients having ingested medicinal doses of iodine, and five fatal cases are cited from the literature.

DULIN, Iowa City.

XERODERMA PIGMENTOSUM: REPORT OF A CASE. CYRIL M. CANRIGHT, Arch. Dermat. & Syph. **29**:668 (May) 1934.

Canright reports a typical case of xeroderma pigmentosum occurring in a Chinese child of 6 years. He gives his report because of the marked rarity of this disease among the Chinese, only one other case having been reported. He notes that the disease is not infrequent among the Japanese. DULIN, Iowa City.

ACNE IN ONE OF IDENTICAL TWINS. W. A. PUSEY and HERBERT RATTNER, Arch. Dermat. & Syph. **29**:706 (May) 1934.

Acne occurred at the age of 23 years in one of identical twins. The twins were similar in all respects except for the acne in the one girl and straighter teeth with fewer fillings in the other twin. It is believed that the predisposing factor for the acne lies in the structure of the skin. It is logical to assume that a difference, analogous to that seen in the teeth, is present throughout the tissues of ectodermal origin and hence in the structure of the skin. DULIN, Iowa City.

XERODERMA PIGMENTOSUM: A STUDY IN SENSITIVITY TO LIGHT. FRANCIS W. LYNCH, Arch. Dermat. & Syph. **29**:858 (June) 1934.

Lynch reviews the cutaneous conditions and diseases brought about by sensitivity to light. He tested the skin for sensitivity to various amounts of ultraviolet rays, with and without special filters, and reports his findings in both the normal child and in the child with xeroderma pigmentosum. A review of the pathology of xeroderma pigmentosum is included. DULIN, Iowa City.

DISORDERS OF THE FEET AS A CAUSE OF RESISTANT ECZEMATOID RINGWORM: THEIR INFLUENCE ON THE AMOUNT OF SWEATING OF THE FEET. THEODORE CORNBLEET, Arch. Dermat. & Syph. **29**:887 (June) 1934.

Resistant eczematoid ringworm and hyperhidrosis of the feet are often associated with orthopedic conditions, such as flatfootedness and the wearing of too short shoes. Both conditions may be cured entirely or at least greatly benefited when properly fitting and orthopedically corrected shoes are worn. Details of an experiment with persons wearing too short shoes, with resultant increase in sweating of the feet, are given.

DULIN, Iowa City.

RINGWORM OF THE SCALP: A REPORT OF THREE CASES DUE TO MICROSPORON LANOSUM WITH A TENDENCY TO SPONTANEOUS RECOVERY. GEORGE M. LEWIS and HELEN C. MILLER, Arch. Dermat. & Syph. **29**:890 (June) 1934.

The importance of making cultures of the offending organism in ringworm of the scalp is emphasized because of the tendency to spontaneous recovery when Microsporon lanosum is present. Three cases of recovery are reported in which general hygienic measures were chiefly responsible for the cure. When cultures are impracticable because of the presence of marked inflammatory reaction, a characteristic of infection with M. lanosum, the tendency in treatment should be conservative; depilating measures or intensive local therapy should be delayed, as the ringworm will probably heal without these.

DULIN, Iowa City.

MULTIPLE BENIGN TUMOR-LIKE NEW GROWTHS OF THE SKIN: REPORT OF A CASE. THOMAS BUTTERWORTH, Arch. Dermat. & Syph. **29**:893 (June) 1934.

Butterworth reports a case of multiple benign tumor-like new growths of the skin occurring in a white girl 11 years of age, which first began to appear at the age of 6 years. The early age of onset is unusual. This disease is not uncommonly associated with syphilis, and although the child's mother was known to have a positive Wassermann reaction at the time of delivery the results of all the serologic examinations for syphilis, including examination of the spinal fluids, were repeatedly negative for the child. All stages of the tumors were to be found, from the beginning of the elevation to the stage where the tumor-like growths had involuted and were replaced by atrophic macules. Photomicrographs of the pathologic sections accompany the article.

DULIN, Iowa City.

VISCERAL MANIFESTATIONS OF ANGIONEUROTIC EDEMA: REPORT OF A CASE WITH RECURRENT PULMONARY INVOLVEMENT. JULIA COLE and HORACE M. KORNS, J. Allergy **5**:347 (May) 1934.

Some of the visceral manifestations of angioneurotic edema are illustrated in the report of a case in a boy 15 years of age, in which recurrent pulmonary involvement, high fever and a predominantly eosinophilic hyperleukocytosis were the outstanding features. The fever was as high as 104 F., and the leukocyte count was up to 62,000, with eosinophils as high as 84 per cent.

HOYER, Cincinnati.

OBSERVATIONS ON SOME DISEASES OF THE SKIN IN INFANCY AND CHILDHOOD. HOWARD FOX, New York State J. Med. **34**:278 (April 1) 1934.

Fox gives an interesting review of diseases of the skin as they occur in childhood. The term birth mark is misleading, as the majority of these marks are not present at birth. As ringworm of the scalp is essentially harmless and nearly always disappears at puberty, it should not be treated with a dangerous drug like thallium acetate. In a study of 28,000 school children in New York City pediculosis was found to be thirty-three times more common in white children as compared with Negroes. "That common warts can be cured by mental suggestion has been

proven beyond question by Bloch in a reasonably large series of cases." Scleroderma of the new-born is exceptionally rare. In many cases this condition can be proved by histologic examination to be necrosis of subcutaneous fat.

AIKMAN, Rochester, N. Y.

ACRODYNIA. L. DE MELLO and JAMES R. WILSON, New York State J. Med. **34**:400 (May 1) 1934.

Two cases of this disease are reported. The patients were sisters, aged 2 and 3 years. Sore throat was present in both.

AIKMAN, Rochester, N. Y.

NEPHRITIS COMPLICATING IMPETIGO. LEE E. SUTTON JR., South. M. J. **27**:798 (Sept.) 1934.

The author reports five cases of children between 3 and 8 years of age in which an eruption of impetigo was followed by acute glomerular nephritis of varying degree and points out the fact that this ordinarily mild disorder can at times be the cause of a serious complication.

SCHLUTZ, Chicago.

THE TREATMENT OF NEVUS VASCULARIS. WILLIAM E. EASTLAND, South. M. J. **27**:802 (Sept.) 1934.

Eastland discusses various methods for the treatment of naevus vascularis. In the majority of such lesions satisfactory results can be obtained. Such treatment requires the attention of the dermatologist or radiologist who has a thorough knowledge of radiotherapy, if unfortunate sequelae are to be avoided and the best results obtained. All physicians practicing obstetrics or pediatrics should have a practical and intelligent knowledge of vascular nevi, thereby enabling them to have their patients so afflicted treated correctly and early in infancy by qualified physicians.

SCHLUTZ, Chicago.

PILI ANNULATI OCCURRING AS A FAMILY DISORDER. ARNE REYN, Brit. J. Dermat. **46**:168 (April) 1934.

Eight cases of pili annulati among four generations in one family are described. A review of the literature revealed twenty cases recorded up to 1921. Other reports of the familial incidence of the condition are reviewed. Reyn believes that the condition is more frequent than the reports in the literature indicate and concludes his article with the statement: "With reference to differential diagnosis there are only a few conditions to be taken into account, foremost of which is monilethrix, as this on cursory consideration may be confounded with pili annulati." A photograph accompanies the article.

WIEN, Chicago. [ARCH. DERMAT. & SYPH.]

CUTANEOUS ENDOTHELIOMA WITH SYSTEMIC MANIFESTATIONS. FRANCO FLARER, Gior. ital. di dermat. e sif. **75**:829 (April) 1934.

A girl aged 16 had cutaneous manifestations consisting of a rounded red tumor of the pubic region, of one and a half years' duration, and of yellowish-red follicular infiltrations resembling the papules of lichen planus on the thorax. Urinalysis and the Wassermann and tuberculin tests gave negative results. The lymphatic glands, liver and spleen were moderately enlarged, and there was slight anemia. Blood smears showed the presence of abundant mononucleated cells. The histopathologic examination of both types of cutaneous lesions revealed the picture of a neoplasm invading the corium and composed of endothelial and lymphoid cells with many newly formed capillaries. Sections of the lymphatic glands showed the same structure. Flarer concludes that the lesions were a neoplastic formation with systemic invasion, arising from the reticulo-endothelial apparatus.

PARDO-CASTELLO, Havana, Cuba. [ARCH. DERMAT. & SYPH.]

Miscellaneous

SIMPLIFIED TECHNIC FOR BLOOD TRANSFUSIONS IN INFANTS. SIDNEY HIRSCH, Arch. Pediat. **51**:264 (April) 1934.

A simple instrument for the administration of citrated blood under controllable pressure through a small needle and therefore especially adapted to pediatric use is described. A V-shaped ground glass adapter with automatic two-way valves is employed with an ordinary syringe. On the upstroke of the syringe the blood is drawn into the barrel and on the downstroke is forced through the opposite arm of the V; valves control this direction of flow automatically, and it is not necessary to remove the syringe during the transfusion.

WADDELL JR., University, Va.

A NEW DEFINITION OF THE NOON POLLEN UNIT. ARTHUR F. COCA, J. Allergy **5**:345 (May) 1934.

A redefinition of the Noon unit is suggested on the basis of the amount of total nitrogen present in the pollen extract. The unit can be defined as the quantity of pollen extract which contains 0.00001 mg. of total nitrogen. This new definition is made because all pollen does not contain the same quantity of hay fever excitant.

HOYER, Cincinnati.

THE BIOLOGIC ACTION OF RADIANT ENERGY: ULTRAVIOLET. EUGENE R. WHITMORE, South. M. J. **27**:796 (Sept.) 1934.

Earlier work failed to confirm previous findings of progressive changes in the internal organs of mice exposed to ultraviolet rays from an efficient quartz mercury vapor arc lamp but showed marked changes in the exposed skin of such mice. This work also showed that mice are not suited for such studies, and it showed the necessity of careful measurement of the dose of ultraviolet radiation, probably of all ultraviolet radiation falling on the exposed surface. The Gordon ultraviolet meter is suitable for this measurement.

Studies of guinea-pigs and rabbits, by measuring the ultraviolet radiation falling on different-sized areas of shaved skin of these animals, show both the guinea-pig and the rabbit to be more resistant to ultraviolet radiation than is the mouse and show both these animals to be suitable for such studies.

As to how ultraviolet radiation acts on the body, it is agreed that it causes typical inflammation in the exposed skin. As to the general body reaction, it is probable that the effects of ultraviolet radiation are produced in a number of different ways not as yet well understood.

SCHLUTZ, Chicago.

THE LESIONS OF ACUTE BARBITURISM. G. CARRIÈRE and C. HURIEZ, Paris méd. **2**:61 (July 21) 1934.

Histopathologic studies based on human material in cases of acute barbital poisoning and on tissues from rabbits experimentally poisoned show the chief lesions to be hyperemia and fatty degeneration. Terminal infections also occur in the liver and digestive tract. In the lung infectious processes occur early, probably favored by the congestion and edema.

LESLIE, Evanston, Ill.

DEVELOPMENT OF THE DENTAL SYSTEM (DEDUCTIONS REGARDING PATHOLOGY). C. RUPPE, Rev. franç. de puériculture **2**:79 (April) 1934.

The development of the dental system explains numerous points in buccal pathology which are interesting because of their relation to the general pathologic conditions of childhood.

CRANE, Chicago.

MEDICAL INSPECTION IN SCHOOLS: WHAT IT SHOULD BE. G. VITRY, Rev. franç. de puériculture **2**:109 (April) 1934.

Medical inspection in schools has been demonstrated to be a necessity. Numerous departments and municipalities in France have already organized this service, and it is expected that it will become obligatory by law. The experience thus far obtained makes it possible to determine accurately the best conditions under which this service should be organized for the most efficacious results.

CRANE, Chicago.

ALLERGIC DISEASE MANIFESTATION. E. LOEWENSTEIN, Wien. Arch. f. inn. Med. **25**:145 (June) 1934.

Parenteral resorption is obligate for the development of allergy in 99 per cent of cases. The disease picture of allergy is determined by the primary portal of entry. The organ system which has primarily been sensitized is also the terrain on which the manifestations of reinfection of allergy manifest themselves. The disease picture of allergy also depends on whether the allergen is of endogenous or exogenous origin. The law of sympathetic inflammation holds for the allergic diseases. In this way one can explain the reoccurrence of particular conditions, such as articular rheumatism, asthma, hay fever, eczemas and various forms of tuberculosis.

The allergy always remains localized in one organ system and is to some extent limited to a specific type of tissue. Allergy can be decreased through (*a*) specific remedies and (*b*) nonspecific remedies. Tuberculous infection causes a constitutional change in the sense that the tendency to inflammation in response to various antigens is increased. The tubercle bacillus seems to be panallergic.

If the antigen circulates in the blood the tendency to inflammation is decreased. It is often observed that a positive tuberculin reaction may disappear during a tubercle bacillemia and does not reappear until some time after the cessation of the bacillemia. The rôle of the complement in the development of an anaphylactic attack must be more thoroughly studied. The sensitivity to toxins also comes within the perspective of allergy.

In all acute and rapidly declining inflammations one must always think of the possibility of an allergic inflammation. The allergic organism possesses in a high degree the capacity to produce connective tissue, whereas the anergic organism has this capacity developed in only a moderate degree. SCHLUTZ, Chicago.

RESULTS OF WORK THERAPY FOR CHILDREN INCAPABLE OF NORMAL OCCUPATIONAL DUTIES. HERMAN WOHLRABE, Ztschr. d. Gesundhführ. **1**:226, 1934.

A certain percentage of all children leaving school must be regarded as physically incapacitated for business life. The chief causes are the poor social conditions which they meet with in their families and a certain degree of constitutional weakness. Hitherto these children have been given short vacations in the country or at the seashore by social service agencies. A new plan has been worked out by which they may be sent to institutions where they are gradually trained to assume normal duties. The idleness consequent to the old methods of giving these children long vacations is probably detrimental. In these institutions the children are given rest and good food but in addition gradually increasing physical duties. This method has led to excellent results. REICHLE, Cleveland.

Society Transactions

SOCIETY FOR PEDIATRIC RESEARCH

Annual Meeting, May 7, 1935

Morning Session

JOSEPH STOKES JR., M.D., *President, in the Chair*

DYSENTERY DUE TO BACILLUS DISPAR. DR. F. F. SCHWENTKER, Baltimore.

Bacillus dispar was cultured from the stools of 36 children with diarrhea. The clinical picture in these cases was fairly characteristic. Fever, toxemia, diarrhea and dehydration were the most constant findings. Stools were frequent and watery and contained mucus but no pus or blood. Twenty-one of the 36 patients died. At autopsy infection of the intestinal mucosa was the only consistent observation; ulceration was not observed.

B. dispar was distinguished from other organisms of the dysentery-paradysentery groups by sugar fermentation reactions as well as by agglutination with specific antiserums. Four of 12 patients tested had in their blood agglutinating antibodies for B. dispar. The development of antibodies was slow and seemed to reach a maximum about five months after the initial illness.

Because of the characteristic clinical picture, the constant association of B. dispar in the stools and the development of specific antibodies in the blood, it was concluded that B. dispar was probably the etiologic agent in these cases of diarrhea.

DISCUSSION

DR. J. D. TRASK, New Haven, Conn.: I am interested in knowing whether it is difficult to develop antiserum in the rabbit. Do you lose many rabbits in the process of immunization?

DR. D. C. DARROW, New Haven, Conn.: I should like to ask whether there was any evidence of carriers or whether the organism was found when there was no clinical disease.

DR. F. F. SCHWENTKER, Baltimore: It is difficult to immunize the rabbits, first, because the organism has low antigenicity and the titer of the antiserum will not go very high. It is usual to get a titer of 160 and occasionally 320. Moreover, the organism carries an endotoxin which may kill the rabbit. We started with minute doses of formaldehydized organisms and in a few rabbits finished up with live organisms. It is difficult to develop a good antiserum and to avoid killing the rabbit.

Search for carriers was made in a few instances. In patients whose stools were cultured on admission to the hospital the presence of the organism was usually associated with evidence of clinical disease. The organism was not found among members of the hospital staff. I do not doubt, however, that carriers exist.

RELATION OF RESPIRATORY INFECTIONS TO RHEUMATIC DISEASE: EPIDEMIOLOGICAL, BACTERIOLOGIC AND IMMUNOLOGIC STUDIES. DR. MAY G. WILSON, New York.

The evidence for the conception of a specific relationship between streptococcic respiratory infections and rheumatic fever is discussed. The validity of the designation "streptococcic respiratory infection" based solely on bacteriologic criteria is questioned. Investigations conducted over a period of years included epidemiological, bacteriologic and immunologic studies of rheumatic subjects from 2 to

15 years of age observed in the homes, wards of hospitals and convalescent cottages. During 1930-1932, 222 ambulatory rheumatic subjects experienced 783 respiratory infections and 401 rheumatic recurrences. It is of some significance that less than 10 per cent of these rheumatic episodes were preceded within a period of three weeks by a respiratory infection.

Close observation of 123 rheumatic children during 1933-1934 included examination of cultures from the throat taken weekly. An analysis of the bacterial flora of the throats of 123 rheumatic children and 109 nonrheumatic subjects for a twelve month period is presented. A total of 6,088 cultures were examined; the relative number of each type of colony was estimated. In addition to the basic pharyngeal flora, which was relatively constant for each person, transient invaders were frequently found and tended to show their maximum incidence at well defined seasons of the year. The seasonal incidence of various organisms in the pharyngeal flora must be considered in evaluating their possible etiologic significance. A comparison of cultures from the throats of rheumatic and nonrheumatic children showed no significant difference in the frequency or time of appearance of hemolytic streptococci in the throat. These findings do not suggest any definite relationship between hemolytic streptococci in the throat and rheumatic fever. During the spring hemolytic streptococci appeared in the pharyngeal flora of the majority of the subjects. It is significant that hemolytic streptococci predominated in the pharyngeal flora of 50 per cent of the subjects during health, of 40 per cent during respiratory infections (majority were common colds) and of 10 per cent during rheumatic activity.

During the year 98 per cent of the children experienced 649 respiratory infections, and 49 per cent suffered from 139 recurrences of rheumatic disease; only 11.5 per cent of the rheumatic episodes were preceded within a month (quiescent period) by a streptococcic respiratory infection.

A correlation of the clinical course with the bacteriologic and immunologic observations on 80 rheumatic subjects from 6 to 15 years of age observed over a period of from twelve to eighteen months is presented. From serial determinations of antistreptolysin during this period basal values for each subject were estimated (the lowest value obtained during a period of apparent health). These values showed a wide range of between 25 and 715 units and remained remarkably constant during periods in which the subjects were free from respiratory symptoms. Following respiratory infections, irrespective of the bacteriologic findings, a rise in titer was consistently, although not invariably, observed. The antistreptolysin curve was characterized by a steplike elevation within one to three weeks after the onset, rising to a peak and either falling by lysis in one to two months or remaining plateau-like for longer periods. Values ranged from 33 to 1,600 units. Two thirds of the subjects experiencing recrudescences of rheumatic disease unassociated with respiratory infection did not show a rise in antistreptolysin titer. The antistreptolysin titer of actively rheumatic subjects experiencing respiratory and streptococcic respiratory infections was similar to that observed for inactively rheumatic subjects experiencing these infections.

Analysis of the data secured did not indicate that the presence of hemolytic streptococci in the pharyngeal flora or the rise of antistreptolysin was necessarily conclusive evidence of a streptococcic respiratory infection. The observations did not seem to support the conception of a specific etiologic relationship between respiratory infections and rheumatic fever.

DISCUSSION

DR. A. A. WEECH, New York: Yesterday we were asked to believe that a discrepancy between the results of two observers might have arisen because of a difference between the guinea-pigs of Boston and the guinea-pigs of New Haven. The findings which Dr. Wilson and Dr. Coburn have reported from observations in New York are clearly not in agreement, and it is difficult to believe that the discrepancy can be accounted for on the basis of a difference in the type of disease

on the east and west sides of the city. I should like, therefore, to say a word in support of Dr. Coburn's observations, for as an onlooker I have been impressed time and again by his ability to predict in advance the occurrence of an acute attack in the subject with previously quiescent rheumatic disease. These children have been sent into my ward without obvious signs of active disease and when it was hard to regard them as potentially ill. And I have watched the predicted flare-up in rheumatic activity develop in one after the other. Because the predictions are so often accurate it is difficult to believe that the data on which they are based can be erroneous. I should like to hear some comment from Dr. Wilson as to how she explains that which seems to be a discrepancy of fact rather than a discrepancy of interpretation.

QUESTION: Will you tell us how Dr. Coburn makes his predictions?

DR. A. A. WEECH, New York: Subjects with quiescent rheumatic disease are followed regularly in a special clinic. During the winter and spring months the chances are better than even that acute infection of the upper respiratory tract with the hemolytic streptococcus will be followed by recrudescence of rheumatic activity. The child may be admitted for observation on the basis of this finding alone. If admission is not possible the patient comes to the clinic at intervals of several days. A sudden upward move in the sedimentation rate or in the antistreptolysin titer presages the impending attack. The sedimentation test is performed immediately at the time of each visit, and the result is known before the patient is allowed to return to his home.

DR. J. D. TRASK, New Haven, Conn.: As I recall, in one of your slides the activity of rheumatic fever appeared fairly constant throughout the year. If I am correct in reading your slide I should like to know what criteria you used for activity.

Second, with regard to the presence of the hemolytic streptococcus in the throat: Did you attempt to quantify the number of streptococci present, and what criteria did you use to decide whether the culture was positive or negative?

DR. W. L. BRADFORD, Rochester, N. Y.: I am interested in Dr. Wilson's discussion of the recurrence of respiratory infections in the patient with rheumatic fever. I wonder whether she has information concerning the incidence of sinus disease in rheumatic children. We find in Rochester that in the rheumatic child it is not unusual to find evidence of sinus infection. We have been somewhat impressed, too, by the variability of the flora in the rheumatic children.

Recently we observed a child with recurrent attacks of rheumatic fever, in whom the flora was pneumococcic and in whose cultures hemolytic streptococci were not demonstrated. In the routine study of our patients with scarlet fever we find that cultures vary tremendously from day to day as regards the presence of hemolytic streptococci, and I suppose that the same variation might occur in the case of the patients with rheumatic fever.

The relationship of rheumatic fever to a nonstreptococcic flora is an exceedingly interesting one.

DR. MAY G. WILSON, New York: I do not think that we can claim differences between the east and west sides of the city, since the majority of these children live on the west side. The types of material are comparable, except for the age group. I suggested to Dr. Coburn that the inclusion of adults in his studies may have influenced his results.

The incidence of rheumatic activity showed an increase in the spring. It was about the same in 1930-1931 as in 1933-1934. It looks much less in comparison with the high incidence of respiratory infection.

Some of the children suffered from chronic sinusitis. In some previous studies we did not find a definite correlation between sinusitis and rheumatic activity.

We followed Brown's classification of streptococci. The relative number of each type of colony was estimated and recorded as 1, 2, 3 and 4 plus. Rheumatic activity included carditis, arthritis, nodules, chorea and pains in the joints.

RECOVERY OF THE VIRUS OF INFLUENZA FROM CHILDREN. DR. I. J. BRIGHTMAN, New Haven, Conn.

During an epidemic of influenza in New Haven and the vicinity during the past winter an agent obtained from the nasopharyngeal washings of children ill with the disease was found which is capable of producing a febrile respiratory infection in ferrets. The agent appeared to have the characteristics of a filtrable virus.

Each of five samples of washings was inoculated in doses of 1 cc. into ferrets by the intranasal route. After an incubation period of from two to six days the animals reacted with symptoms of an acute respiratory infection accompanied by a diphasic rise in temperature. Recovery occurred in from eight to twelve days, with the development of an active immunity lasting at least two months. The disease could be passed in series from ferret to ferret by transfer of nasal washings or suspensions of the lungs of sick animals. Filtered suspensions, proved to be bacteria-free by aerobic and anaerobic methods of culture, were effective in continuing the passages. Pulmonary disease developed by the second or third animal passage and consisted at first of patchy consolidations which later in the series became confluent. These lungs were free from bacteria in all but a few of the ferrets in which later passage was carried out, which were secondarily invaded by hemolytic streptococci. The virus could be recovered from such lungs by filtration.

Ferrets inoculated with cultures from the nose and throat of both normal persons and persons with minor respiratory infections showed no symptoms at any time.

Nasopharyngeal washings from a person with a common cold and from six children in the preeruptive stage of measles failed to produce a reaction in ferrets on intranasal instillation.

Suspensions of ferret lung containing the "influenza virus" have produced a disease in white mice characterized by definite pulmonary lesions and fatal termination. Guinea-pigs and rabbits proved refractory to the virus.

These studies have corroborated those of other investigators, notably of Smith, Andrews and Laidlow and of Francis, in pointing to a filtrable virus as the causative organism of influenza.

EFFECT OF PURIFIED DIETS ON THE RESISTANCE TO INFECTION IN MICE. DR. C. F. CHURCH, Philadelphia.

Resistance of the host to infectious disease has been shown experimentally to be influenced by heredity and by diet. Webster has developed pure lines of "susceptible" and "resistant" mice and a technic for measuring the resistance of a previously unexposed progeny to a specific infecting organism introduced in uniform dosage through the natural portal of entry.

Using these homozygous lines of mice and the technic referred to, a study is now being made of the effect of various purified diets on resistance to mouse typhoid infection with Bacillus enteriditis. The curves for mortality obtained by Webster on susceptible and resistant progenies maintained on the same diet, a modified Steenbock ration, have been duplicated. A synthetic diet of purified food elements, which has proved adequate for growth and reproduction, has been compared with the Steenbock diet. The characteristics of the curves for mortality were similar, but a significant difference in morbidity was demonstrated. Recovery of the infecting organism in pure culture from the tissues at necropsy is a routine step in establishing the cause of death.

This new diet will serve as the basis for future modifications planned with the objective of discovering what dietary element or elements are responsible for alterations in natural resistance.

LYSOZYME CONTENT OF BLOOD. DR. J. ROBERTS and DR. W. L. BRADFORD, Rochester, N. Y.

In 1921, Fleming described a substance widely distributed in the tissues of animals and in plants which possessed a remarkable lytic effect on certain organ-

isms. His work led him to believe that the substance was similar to an enzyme; accordingly he named it lysozyme, and the susceptible organism—a micrococcus isolated from the nasal mucous membrane of a person suffering from coryza—he called Micrococcus lysodeikticus. Lysozyme in varying concentrations was demonstrated in the organs and body fluids of man; tears, spleen, liver, lung and cartilage were found to be particularly active. Blood serum, as well as leukocytes, contained it, and it was suggested that lysozyme might play an important part in phagocytosis and therefore have immunologic significance. Since the discovery of this substance its relationship to several clinical conditions has been studied. This report deals with the results of an investigation on the lysozyme content of blood.

Method.—During the first part of the work serum was used in dilutions ranging between 1:5 and 1:160. Twenty-four hour growths of M. lysodeikticus were washed from agar slants with physiologic solution of sodium chloride, standardized to match the turbidity of a no. 9 barium sulphate standard and preserved with a 1:10,000 solution of merthiolate.

To a series of tubes containing dilutions of serum equal amounts of the suspension of the organism (0.5 cc. of serum + 0.5 cc. of the suspension of the organism) were added. The mixtures were then incubated for twenty-four hours in a water bath at 37 C., and readings to determine the degree of clearing were made against a blue light. Results were recorded as complete, incomplete and no lysis.

After the work was in progress it was learned that the lytic property of blood was of greatest concentration in the leukocytes. The method was therefore modified to permit an investigation of the lytic substance contained within a given sample of leukocytes. For this purpose .5 cc. of blood was mixed with 0.010 Gm. of potassium oxalate. The blood was centrifugated and the leukocyte layer removed and mixed with sterile distilled water. The number of leukocytes in the first tube was then adjusted to approximately 4,000,000 per cubic centimeter. Serial dilutions were made and the process completed as described. Films were made from the samples of blood; these were treated with Wright's stain, and differential counts were made.

Results.—When the serums of 9 normal children were tested in dilution, 3 gave complete lysis in a dilution of 1:5 and 2 in a dilution of 1:20.

In other conditions the results were as shown in the table.

Highest Dilutions of Serum Showing Complete Lysis

	1:5	1:10	1:20	1:40	1:80	1:160
Cord blood (33)	27	23	9	3		
Pregnancy (11)	11	4	3			
Pneumonia (8)	3	2				
Rheumatic fever (5)	3	3	2	1		
Scarlet fever (17)	7	6	2			

When inactivated serum (exposed to a temperature of 56 C. for thirty minutes) was used lysis was reduced. Of 33 samples of cord blood 5 showed complete clearing in the 1:5 dilution; 4 in the 1:10 dilution; 2 in the 1:20 dilution, and 1 in the 1:40 dilution. In 22 cases of diabetes none revealed complete lysis. In 14 cases of congenital syphilis lysis was complete in the 1:5 dilution three times, while in 6 cases of cancer and in 19 cases of pregnancy there was no instance of complete lysis.

When dilutions of suspensions of leukocytes were tested the lytic effect was more pronounced. In the blood taken at the height of scarlet fever, rheumatic fever, lobar pneumonia and measles and after artificial fever therapy the lysozyme content of the mixtures was definitely increased. In whooping cough and in lymphatic leukemia it was decreased. In lobar pneumonia a marked decrease was observed after the crisis occurred. Differential counts indicated that the more active mixtures

contained the highest percentage of polymorphonuclear leukocytes. This was confirmed when the titer of a pleural exudate (91 per cent polymorphonuclears) produced in a rabbit with aleuronat was compared with that of one produced with a mixture of beef extract and acacia (30 per cent polymorphonuclears) and with a phosphorus peritoneal exudate from a guinea-pig (10 per cent polymorphonuclears). Tabulation of the results obtained in 157 tests on suspensions of leukocytes indicated that there was a direct correlation between the degree of complete lysis and the percentage of polymorphonuclears in the mixture.

From the results of this investigation it would seem that in blood the lysozyme titer is dependent on the number of leukocytes and is particularly a property belonging to the polymorphonuclear element.

DISCUSSION

DR. L. E. HOLT JR., Baltimore: I should like to ask Dr. Bradford whether he made any correlations between the lysozyme activity and the maturity of the leukocytes.

DR. R. MCINTOSH, New York: I should like to ask Dr. Bradford whether it is not possible that he is working with two factors: one that may be in solution, as in lacrimal secretion and plasma, the other within the polymorphonuclear leukocytes. Is it possible to differentiate the two?

DR. W. L. BRADFORD, Rochester, N. Y.: In answer to Dr. Holt's question, we have made no investigation to correlate the age of the leukocyte with its lysozyme content. In a case of myelogenous leukemia in which many myeloblasts were demonstrated the lysozyme was very inactive, although we adjusted the first tube to contain 9,000,000 leukocytes.

In answer to Dr. McIntosh's question, it is probable that more than one lytic substance may be present. It is difficult, however, to obtain purified lysozyme from blood, as Wolff did from egg white. The bacteriolysins of serum differ from lysozyme, but in leukocytes such thermostable substances as leukins may have a similar action.

In this work the term lysozyme is applied broadly to that substance capable of lysing the Fleming organism. It is interesting to observe that the content of leukocytes is so high, in view of the fact that the leukocyte is also the home of several other enzymes.

BLOOD COAGULANTS FROM PLACENTAL EXTRACTS; EFFECT IN HEMOPHILIA. DR. R. C. ELEY, DR. A. A. GREEN and DR. C. F. MCKHANN, Boston.

Studies have been made with a tissue protein derived from human placentas in an effort to determine similarities or differences in the coagulative action on the blood of this and of extracts of animal tissues. The coagulative action of extracts of animal tissues has been studied by Wooldridge, Loeb, Ichikawa, Mills, Torraca and others. That tissue coagulants have some degree of specificity for the species from which they are derived has been suggested by Loeb and Mills. Consequently it seemed possible that one might obtain a more effective coagulant for man by the employment of a tissue protein extracted from human tissue. Observations on the coagulant action of placental extracts have been made by Sakurai. Our studies have confirmed and extended his work.

In vitro experiments have shown that an extract from the human placenta possesses a coagulant action which retains its potency when the extract is employed in high dilutions. It appears to be more effective as a coagulant than the substances now available. Like other tissue extracts, the coagulant qualitatively is nonspecific for species. Studies on the relationship of the concentration of tissue coagulant to the coagulation time of recalcified plasma have shown that the coagulation time approaches a limit where no further reduction occurs as one increases the concentration of tissue coagulant. The tissue coagulant clots hemophilic blood as rapidly as normal blood. In addition to shortening the time of coagulation the

extract exerts an influence on the weight of fibrin formed from the plasma of either man or animals according to the amount added to the plasma. The increase in weight of the fibrin obtained from the clot is proportional to the amount of protein added. Thus it appears that tissue coagulants enter into the actual formation of fibrin.

The substance injected intraperitoneally into rabbits in amounts of 1 cc. brought about a reduction in the coagulation time of both the venous and the capillary blood. This reduction persisted for periods varying between forty-eight and seventy-two hours.

The extract was given to a normal person by the method of Mills; 5 cc. of the extract was given on an empty stomach; a glass of ice-cold water was given before and after. Thirty minutes later the clotting time of the venous blood had been reduced from six and one-half minutes to one minute and twenty-five seconds, and the clotting time of the capillary blood had fallen from two and one-half to one and one-half minutes. At the end of five hours it was observed that the coagulation time was gradually becoming prolonged, and at seven hours the coagulation time had reached the normal level.

In 1931, Eley and Clifford confirmed the observations of Vines and Mills on the treatment of hemophilia by protein sensitization. At that time it was noted that the reduction of clotting time applied only to the capillary blood and not to the venous blood, as the coagulation time of the latter remained unchanged. Since an extract of tissue prepared from human placentas had been found to possess a coagulant action effective on both venous and capillary blood when administered intraperitoneally to animals and by mouth to man, determination of the effectiveness of this substance in patients with hemophilia was made.

Ten patients suffering from hemophilia have been given placental tissue protein by oral administration in an effort to determine the effect on the coagulation time of both the capillary and the venous blood. The extract has been given after a period of fasting, and ice-cold water given before and after; it has also been given with alkaline carbonated water or with sodium bicarbonate. In 8 of the patients a reduction of the venous and the capillary clotting time to normal limits has been obtained. The duration of the effect was from two to seven days. Two patients have failed to show a definite response. From these results it can be seen that although there has been a reduction in the coagulation time of both the venous and the capillary blood, the effect has not always been adequate; nor have we been able consistently to reduce the coagulation time in the same patient. The effect of the extract given orally during attacks of bleeding has not been ascertained.

These studies have not answered the questions as to whether the homologous nature of this coagulant renders it superior to the similar coagulants derived from various animal tissues. If a superiority is found a method of administration which will lead to uniform and dependable results must be sought, and the possibility of deleterious effects on patients must be further investigated. Means must be found to preserve the material from loss of potency.

DISCUSSION

DR. G. M. GUEST, Cincinnati: In one of the slides, I believe, you showed that the placental protein given in alkaline solution by mouth brought down the venous clotting time, whereas the lung extract did not. Was the lung extract given in Vichy water?

DR. R. C. ELEY, Boston: We gave it both ways, first with cold water and subsequently with alkaline Vichy water as well.

DR. L. E. HOLT JR., Baltimore: I should like to ask what is the lipid content and the nature of the lipids in this extract.

DR. J. STOKES JR., Philadelphia: I should like to ask whether this material was given by a duodenal tube, and if so, whether there was any rough quantitative relationship between the amounts absorbed when given by mouth and the amounts absorbed when given by the duodenal tube.

Dr. A. A. Weech, New York: In some cases of prolonged coagulation it is not clear whether the delay results from a lowered amount of thrombin in the blood or from an increase in antithrombin. Will the extract produce a reduction in the coagulation time of blood to which an anticoagulant has been added?

Dr. G. M. Guest, Cincinnati: Recently there has been a considerable amount of discussion of the apparent benefit of injections of theelin in hemophiliacs. Is there any reason to believe that there may be such a hormone extracted from the human placenta and included in your extract, having an additive effect augmenting that of the tissue protein coagulant when the latter is given to the hemophiliacs in the manner that you have described?

Dr. R. C. Eley, Boston: The extract does contain a lipin. I cannot answer the question as to the quantitative relationship. We have not given the extract by duodenal tube, although we have given it by rectum and obtained results similar to those obtained when it is administered by mouth.

As to Dr. Weech's question as to whether or not the extract will produce reduction in the coagulation time of blood to which some anticoagulant has been added, the extract has been added to blood containing both sodium citrate and heparin, and in each instance there has been a reduction in the coagulation time.

Repeated attempts to demonstrate the presence of any female sex hormone in the extract have always been negative.

Dr. C. F. McKhann, Boston: In regard to Dr. Guest's statement concerning the use of ovarian extracts in hemophilia a survey of the several studies of the use of ovarian extract indicates that the cruder extracts were the more effective. As purified hormone preparations have failed to work, it is possible that any activity of crude ovarian extracts may be due to the inclusion of ovarian tissue proteins which would have the effect of a tissue coagulant. The placental tissue proteins which we have studied have not contained female sex hormones.

The material does contain a lipin—a phospholipin, to which part of the activity may be attributed. However, the phospholipin alone is not as effective as the combination of the lipin with the proteins. The quantitative relationships of this phosphorus-containing compound have not been worked out.

Blood Fibrin Studies in the New-Born. Dr. M. J. E. Senn, New York.

This paper will be published in full in the *Journal of Pediatrics*.

DISCUSSION

Dr. A. A. Weech, New York: This particular aspect of the general problem which Dr. Senn has studied, namely, whether it is worth while to administer gelatin solution to new-born infants, is worthy of comment.

About two years ago Dr. Davidson and Dr. Merritt at the Babies Hospital made some observations on the effect of administering a gelatin solution to new-born infants. Like Dr. Senn, they found that the babies gained in weight and that some of them showed subcutaneous edema. In two instances it was possible by puncture of the subcutaneous tissue to collect enough edema fluid for analysis. These fluids contained between 1 and 2 per cent of protein. This is the type of edema fluid which occurs when there has been injury of the capillaries. A gain in weight resulting from damage to the capillaries cannot be regarded as desirable.

Respiratory Metabolism in Infancy and in Childhood: XVI. Effect of Intravenous Infusions of Fat on the Energy Exchange of Infants. Dr. H. H. Gordon and Dr. S. Z. Levine, New York.

This paper appeared in full in the October 1935 issue of the American Journal of Diseases of Children, page 894.

DISCUSSION

Dr. I. McQuarrie, Minneapolis: I should like to ask Dr. Gordon what is the greatest amount of fat one can safely inject in emulsion form and what fats in general are most desirable.

DR. L. E. HOLT JR., Baltimore: I wish to express my appreciation of the work that Dr. Gordon has done; it is work that we were incapable of doing in Baltimore. I wonder whether he would care to say anything about the observations that he has made in regard to the excretion of ketone bodies after intravenous injections of fat.

DR. H. GORDON, New York: In answer to the first question, I can say only that the largest infusion that we have given was 200 cc. of a 5 per cent emulsion to an infant weighing approximately 8,000 Gm., with no harmful effects. I do not know how frequently such a procedure can be repeated without harm. Dr. Holt can probably give more information concerning that question and also the types of oils used.

Our experiments with the excretion of acetone following infusions of olive oil have given only enough information to warrant our being willing to continue further with them.

BETA HEMOLYTIC STREPTOCOCCIC INFECTION IN INFANCY AND CHILDHOOD: I. ANTIFIBRINOLYSIN AND ANTISTREPTOLYSIN RESPONSE. DR. V. W. LIPPARD, New York.

This article was published in full in the June 1935 issue of the AMERICAN JOURNAL OF DISEASES OF CHILDREN, p. 1411.

DISCUSSION

DR. J. D. TRASK, New Haven, Conn.: It is strange that the blood of new-born infants resists the lysis of the clot so well. Accordingly, I should like to know whether the mothers were infected with hemolytic streptococcus, or whether there was anything that led you to believe that there were two mechanisms at work in delaying the lysis of the clot?

The next question is one of technic. How do you keep your cultures so as to give rise to standard conditions?

DR. V. W. LIPPARD, New York: The mothers from whom the blood was selected for titration were in good health and had recently delivered normal infants. None of them had recently recovered from infection due to the hemolytic streptococcus. Specimens of blood from a group of these mothers were found to have a low resistance to the fibrinolytic action of hemolytic streptococci, while their infants often had a very high resistance on the first day of life. Although we have no data to substantiate it, one might be led to believe that the substance in the blood of the day old infant which inhibits fibrinolysis may not be the same as that which appears later in life.

The substance in the blood of new-born infants which inhibits fibrinolysis does not seem to protect them from infection by the hemolytic streptococcus. The anti-fibrinolytic substance in the blood of infants in whom infections did not develop during the first few days of life promptly diminished soon after they became infected either with hemolytic streptococci or other organisms. That may account for the rapid dissemination of erysipelas in new-born babies.

The cultures of hemolytic streptococci used in these experiments were obtained from persons with acute infections, grown in beef heart infusion broth and transferred daily. In order to determine whether or not they maintained constant fibrinolytic activity they were tested at about weekly intervals against the plasma of persons who remained free from infection by the hemolytic streptococcus. The activity remained fairly constant during the period of study. Each specimen of plasma was tested against three cultures of approximately equal potency.

DETERMINATION OF THE SEPARATE FRACTIONS OF THE BLOOD LIPIDS BY A MICRO-GRAVIMETRIC TECHNIC. DR. W. R. WILSON and DR. A. E. HANSEN, New Haven, Conn.

Heretofore it has not been possible to study the various fractions of the blood lipids with the small quantities of material that are available. The desirability of such a method, particularly as regards the saponifiable fraction, is evident. The present method is based on an early study of Bloor, in which large quantities

of blood were used, and on the microgravimetric technic of Wilson and Hanner for the determination of the total lipids.

The alcohol-ether extract of the blood or serum is prepared in the usual manner and saponified with potassium hydroxide, and hydroquinone is added to prevent oxidation. After acidification the lipids are extracted with petroleum ether; the volume is reduced by evaporation, then the extract is resaponified with alcoholic potassium hydroxide. Water is added, and the mixture is emulsified by stirring. The soaps remain in the alcohol-water layer while the supernatant petroleum ether layer contains the unsaponifiable lipids. The unsaponifiable portion is transferred by means of a rubber bulb pipet with a capillary tip to a tared weighing bottle. The saponified portion again is protected with hydroquinone and evaporated to dryness. The soaps are then dissolved in water, acidified and extracted with petroleum ether as already described and transferred to a tared weighing bottle. Hydroquinone is added to the fatty acid fraction, which is evaporated to dryness and weighed.

The titration value of the isolated fatty acid fraction is obtained by titrating in hot alcohol with sodium hydroxide, using phenolphthalein as an indicator. The average molecular weight is calculated from the titration value and the weight. After evaporation of this material to remove all the alcohol, it is acidified and extracted with petroleum ether. The iodine absorption capacity is determined on the same specimen.

In this way the unsaponifiable and saponifiable portions of the blood lipids are determined separately. The titration value, the milliequivalents of fatty acid, the average molecular weight, the average iodine value and the number of double bonds per molecule of the fatty acids are obtainable.

Known solutions of mixtures of linoleic acid, palmitic acid and cholesterol were determined by this technic, with values for the weights, the titration value, the average molecular weight and the average iodine number that checked within 2 per cent.

Determinations of the serum lipids in 17 normal persons revealed values which are in essential agreement with those found by other methods.

Afternoon Session

CHARLES F. MCKHANN, *Vice President, in the Chair*

TOTAL ELECTROLYTE CONTENT OF ANIMALS AND ITS PROBABLE RELATION TO THE DISTRIBUTION OF BODY WATER. DR. H. E. HARRISON, DR. D. C. DARROW and DR. H. YANNET, New Haven, Conn.

Except for the red cell, it is not possible to examine intracellular material directly with any degree of accuracy. In the present communication an attempt is made to approach this problem indirectly. Certain considerations are suggested which lead to the conclusion that the chloride ion is almost entirely, if not exclusively, extracellular. A series of calculations based on this assumption have been outlined. As a result of the application of these calculations to data obtained by the direct analysis of the body tissue of 3 rabbits, 2 monkeys and 1 dog, the following information was obtained:

1. The concentration of intracellular potassium in the body tissues is of almost the same magnitude as the concentration of sodium + potassium in the red cell, namely, about 140 milliequivalents per liter of water.

2. The extracellular fluid made up about 25 per cent of the body weight of the animals examined, a value which agrees with that determined by means of the sulphocyanate method by Crandall and Lavietes and Peters.

3. The concentration of protein in the muscle cell is of about the same magnitude as the concentration of protein in the red cell, namely, from 30 to 33 per cent.

4. About 75 per cent of all the sodium in an adult animal is present in the extracellular fluid. The remaining fraction is found almost entirely in the skeleton and probably exists in the form of a salt which is to a large extent nonionizable.

The distribution of water in the body and the concentration of cations in the intracellular and extracellular water agree so well with present conceptions of the osmotic relationships that should obtain that we believe that our original assumption, namely, the exclusively extracellular distribution of chloride, may serve as a first approximation for future investigations.

DISCUSSION

DR. A. M. BUTLER, Boston: I should like to ask whether Dr. Yannet, Dr. Harrison and Dr. Darrow have made any direct analyses of bone. We have made some analyses of bone and found that the sodium reported in bone by their indirect analyses is there on direct analysis. Moreover, if one grinds up bone and extracts it with water, sodium is still present in the insoluble bone residue and, to our astonishment, if one takes ashes of an animal and dries them with sulphuric acid not only is sodium present in the water-insoluble calcium-phosphate residue, but it is present in this residue in a form which is insoluble in dilute nitric acid.

DR. H. YANNET, New Haven, Conn.: I have no clear idea how this sodium is present in the bone. We plan to work on that problem at the present time because of the importance that it may assume in evaluating the results in studies of the sodium balance under varying conditions.

We have not had an opportunity to examine bone, except in the experiments reported. We intend to do that, too, on different animals to see whether this finding will be confirmed.

VAPOR PRESSURE OF WHOLE BLOOD AND SERUM IN THE NORMAL AND DEHYDRATED CHILD: TECHNIC AND MEASUREMENTS. DR. R. W. CULBERT, New York.

The vapor pressure of defibrinated whole blood of 50 infants and children was determined by the thermo-electric method devised by A. V. Hill and utilized by R. Margaria in 1930, when he determined the vapor pressure of adult defibrinated blood. Gilman and Cowgill and their associates have used the method in determining the vapor pressure of simultaneously collected samples of dog blood and other biologic fluids such as bile and lymph.

The method depends on the difference in temperature attained by opposite faces of a symmetrically wound thermopile on one face of which is a filter paper saturated with the defibrinated blood, while on the other is placed a similar piece of filter paper soaked in a standard solution of sodium chloride. The difference in temperature resulting from the unequal rates of evaporation on the two faces produces an electromotive force which is read on a sensitive galvanometer. The thermopile having been calibrated with solution of sodium chloride of accurately known concentration, the vapor pressure of the blood can be calculated in terms of the standard solution. In order to avoid the error which may occur because of the loss of carbon dioxide from the sample of blood, a mixture of 5 per cent carbon dioxide and 95 per cent oxygen, after saturation with moisture at the temperature of the bath (25 C. $\pm$ 0.001 C.), was introduced into the thermopile chamber.

The average vapor pressure of 50 samples of blood, as equivalent grams per hundred cubic centimeters of sodium chloride, was 0.9029, with a standard deviation of 0.0171. No statistical difference could be shown between the blood samples of 30 boys and 20 girls ranging in age from 1 month to 12 years. Twenty-six samples of serum from blood collected under oil gave an average value of 0.8545 with a standard deviation of 0.0166 in equivalent grams per hundred cubic centimeters of sodium chloride while 10 samples of spinal fluid gave a similar average value of 0.8532 with a standard deviation of 0.0127. These are considered normal values.

Marked deviations from the normal were obtained in cases of acute intestinal intoxication, but the direction from the normal could not be predicted. Thus, in one case there was a 37 per cent increase in the vapor pressure of whole blood, while in another case in which the patient presented similar symptoms there was a 6 per cent decrease below the normal.

DISCUSSION

DR. L. E. HOLT JR., Baltimore: I should like to ask Dr. Culbert how large a sample is required to make this determination.

DR. D. C. DARROW, New Haven, Conn.: I should like to ask him why the serum vapor pressures are different from those of the whole blood.

DR. B. HAMILTON, Chicago: I should like to ask whether determinations of total fixed base were also made and, if so, whether there was a good correlation between fixed base and osmotic pressure.

DR. R. W. CULBERT, New York: 1. Approximately 1 cc. of serum or other biologic fluid is used in making two double determinations. Half this amount may be used for a single double determination but, as has been shown, the error is somewhat increased.

2. When 5 per cent carbon dioxide is added to the system there is a measurable increase in total osmotically active substance. This is considered to be due to the effect of carbon dioxide on the hemoglobin of the red cell. The shift of anions from cells to plasma and vice versa, as well as the shift of water to maintain an osmotic balance, appear to be linked with the quantity of hemoglobin present, the total fixed base remaining constant.

3. The determination of total base with parallel measurements of vapor pressure in samples of serum collected under oil is now being undertaken. While this work is not yet completed, it may be said in general that when other factors are not operating to modify the readings, the changes in vapor pressure parallel those which occur in total base. However, abnormal values of nonprotein nitrogen seem to modify the readings for the vapor pressure, even when the figures for the total base show no variation from the normal.

NATURE OF THE SERUM PROTEINS IN NEPHROSIS. DR. ELVIRA GOETTSCH, New York.

Specific antiserums were developed in rabbits by immunization with albumin and with globulin isolated from pooled human serum. By means of the quantitative precipitin method the antiserums were used to measure the albumin and globulin in the serums of normal human beings and of patients with edema from other causes than nephrosis. In these cases the total protein of the serum, calculated from the protein nitrogen, was approximately the same as the sum of the values for albumin and globulin obtained by the precipitin method. In a larger series of dogs similar results were obtained; i. e., the total protein content of serum could be determined satisfactorily by the quantitative precipitin method in normal dogs and also in the same dogs after edema had developed with a diet low in protein.

Six patients with nephrosis were studied. During the edematous stage a very small fraction of the serum albumin and only half of the serum globulin could be precipitated with the specific rabbit antiserums. After recovery, in the two patients with whom prolonged study was possible both albumin and globulin could be precipitated like the proteins of normal serum. The change in the immunologic reaction of the serum globulin occurred shortly after diuresis began; the return of the serum albumin to normal required a longer time. Because of this constant variation the total protein could not be estimated satisfactorily in the nephrotic patient until recovery occurred.

Similar changes were not found in the serum proteins of a series of patients with acute glomerular nephritis.

Extraction of the serum of the patients with nephrosis with ethylene chloride removed the cholesterol but had no effect on the precipitin reaction, which indicates that the failure of this serum to react with the antiserums is not due to its high cholesterol content. The addition of the serum of patients with nephrosis to normal serum did not interfere with the complete precipitation of the normal proteins. When rabbits were immunized with serum globulin isolated from the serum of

patients with nephrosis an antiserum was obtained with which it was possible to determine the globulin in the serum of patients with nephrosis quantitatively, both during the edematous stage and after diuresis had occurred.

DISCUSSION

DR. B. KRAMER, Brooklyn: I should like to ask Dr. Goettsch whether the proteins which she isolated from the urine of patients with nephrosis differed in their physical properties from the albumins and globulins found in normal serum.

DR. ELVIRA GOETTSCH, New York: We did not determine the physical and chemical properties of the serums from the patients with nephrosis. Other workers, who measured the optical rotation and racemization curves, found no differences between normal serum proteins and serum proteins from patients with nephrosis.

NITROGEN, CALCIUM AND PHOSPHORUS BALANCES OF INFANTS FED SWEETENED CONDENSED MILK AND EVAPORATED MILK. DR. H. E. HARRISON, New Haven, Conn.

The retentions of nitrogen, calcium and phosphorus of 5 infants ranging from 3 to 7 months of age were determined in relation to two types of feeding differing in their content of protein. The feeding mixtures used were sweetened condensed milk which supplies 10 per cent of its calories in protein and diluted evaporated milk with 6 per cent added sucrose, supplying 15 per cent of its calories in protein. Both types of feeding were supplemented with orange juice and cod liver oil. This study was done because of the usual teaching that an intake of protein equivalent to only 10 per cent of the total calories is inadequate for artificially fed infants.

In these experiments just as high retentions of nitrogen were found with the sweetened condensed milk as with the feedings of evaporated milk and sucrose. The retentions of calcium and phosphorus were somewhat greater with the feeding of evaporated milk and sucrose. It was concluded that the retentions of nitrogen, calcium and phosphorus observed in infants fed sweetened condensed milk were sufficient to permit normal growth.

DISCUSSION

DR. L. E. HOLT JR., Baltimore: I should like to ask Dr. Harrison how his figures for nitrogen retention compared with those of Dr. Swanson. I was under the impression that Dr. Swanson obtained higher figures for nitrogen retention in babies who were artificially fed than in breast fed infants.

DR. W. W. SWANSON, Chicago: The nitrogen retention for infants for each kilogram of increase in weight was 2,600 millimols of nitrogen for those on cow's milk and 1,700 millimols for those on breast milk. On the whole, an infant on cow's milk retains about 50 per cent more nitrogen.

We found also a marked increase in the retention of calcium in infants on cow's milk. After cod liver oil was taken, there was a marked increase in the calcium retention in both infants on cow's milk and those on breast milk. However, the difference in the percentage retained was approximately the same.

DR. S. Z. LEVINE, New York: I was exceedingly interested in Dr. Harrison's paper because it more or less agrees with the data that we have been collecting in the past and present.

Apparently, the reservoir, if one can use the term, for protein in the infantile organism is limited, despite the fact that the infant is a growing mechanism. I was interested to know whether Dr. Harrison believes that if the condensed milk formula were used in larger amounts, or, to put it another way, if the intake of protein remained the same with an increase in total calories, one might not expect to get an increased nitrogen retention, even with the minimum intakes. I think that when one gets above a certain maximum the infant apparently protects itself by not storing protein commensurate with the increased intake.

The same, of course, applies to carbohydrate. One cannot load up the infantile organism by increasing the intake of carbohydrate. The only limitless store or reservoir for organic material in the infantile organism is fat, as in the adult.

DR. D. C. DARROW, New Haven, Conn.: I have talked over these findings with Dr. Harrison. I do not know whether he thought it worth while to bring out that the infant who had a low retention during the period when condensed milk was fed showed evidence that he was not yet in equilibrium on this diet. The day-to-day retentions of nitrogen were increasing during this period so that for the last three days of the seven day period they were at a level which would give the same nitrogen retention as was obtained on the high protein diet.

A recent publication in Germany reports similar results. Nitrogen retentions over a period of fifteen days were studied in infants fed breast milk followed by isocaloric amounts of cow's milk plus sugar. With mixtures of cow's milk more protein was given, and during the first three to four days more nitrogen was retained. Later the excess of nitrogen was excreted, so that the retentions over the periods of fifteen days were substantially the same as with breast milk.

I think that the older idea that nitrogen retention can be increased by increased intake of protein is based on two errors in collecting data. First, the experiments were run before equilibrium had been established. Apparently a certain lag in establishing an equilibrium exists when changing from a high to a low protein diet or vice versa. However, after a diet is consumed for a period of time retentions become fairly constant.

In previous experiments the other variable that was not kept constant was the caloric intake. If one increases the caloric intake without altering the intake of protein, the retention of nitrogen will probably increase.

DR. H. E. HARRISON, New Haven, Conn.: In regard to Dr. Holt's question, Dr. Swanson found a daily retention of 0.96 Gm. in infants who received a preparation of cow's milk and, I think, about 0.6 Gm. in infants who received breast milk. Two of our own infants fed sweetened condensed milk showed equal or higher retentions. Three showed somewhat lower nitrogen retentions. Dr. Swanson's work was carried out on only one infant. We do not know what a whole group of infants might show.

We also thought that the caloric intake was the deciding factor in the nitrogen retention until one got down to a definite minimum of protein. By increasing the caloric intake one probably could increase the nitrogen retention, even with a low level of intake of protein, but we thought that increasing the intake of protein above the minimum of protein without increasing the calories would have no influence on increasing the nitrogen retention.

RELATION OF VITAMIN B TO FAT METABOLISM. DR. DOROTHY V. WHIPPLE and DR. C. F. CHURCH, Philadelphia.

Experiments in this laboratory have shown that synthesis of the antiberiberi factor in the gastro-intestinal tract of an animal receiving no vitamin B_1 in its diet is possible only in the presence of dietary fat. Other experiments suggest that the synthesis of fat in the tissue of a rat on a fat-free diet is possible only in the presence of vitamin B_1. The addition of fat to a diet free from vitamin B_1 spares the vitamin, but the converse is not true; large additions of vitamin B_1 do not spare fat in a fat-free diet.

DISCUSSION

DR. W. M. SPERRY, New York: I should like to ask whether the so-called sparing action of fat on vitamin B can be explained in a way by these findings. If one of the functions of vitamin B is to catalyze the synthesis of fat from carbohydrate, as this paper indicates, less vitamin B might be needed when adequate fat is given in the diet. I should appreciate Dr. Whipple's comment on this point.

DR. G. M. GUEST, Cincinnati: I understand that, from evidence given by the sugar tolerance curves, it was concluded that there was no lack of insulin, and it was consequently postulated that the metabolic defect lay in the conversion of

carbohydrate into fat. The theoretical approach seems to have bridged a wide gap, and one might ask whether the intermediate carbohydrate metabolism has been fully considered. Could not defective conversion of glycogen be postulated equally well to explain the reported findings?

DR. I. MCQUARRIE, Minneapolis: I should like to ask Dr. Whipple whether she analyzed the livers of these rats for fat.

DR. S. Z. LEVINE, New York: In line with Dr. Guest's suggestion, one way of arriving at the alternative possibility would be to determine respiratory quotients. If in the rats with vitamin A deficiency one never could get a quotient above 1 with these diets and if in the control rats one did, it would give, it seems to me, fairly direct evidence regarding his theory as opposed to the other.

DR. E. A. PARK, Baltimore: I wish to ask Dr. Whipple why the animals lost weight. They did not lose weight because they could not store fat.

DR. DOROTHY V. WHIPPLE, Philadelphia: The question of respiratory quotients is on our program for the immediate future. We have not as yet had time to carry out such studies.

On the question of our theoretical approach, there may be other possible explanations. Storage of glycogen may indeed be a factor. We thought, however, that the synthesis of fat was a reasonable explanation and formulated our present hypothesis. The experimental results which we have just reported lend support to the hypothesis. There is still much to be done.

Concerning Dr. McQuarrie's question about the liver, we have analyzed the livers separately in all these animals. We found certain differences which are consistent, but they certainly are not striking. The differences in deposition of fat in the total carcass and in the skin are far greater than the differences in the liver fat.

Regarding Dr. Sperry's question, concerning the sparing action of fat on vitamin B, I am not quite certain, but it may be possible that this function of vitamin B which we have reported, namely, the ability to permit the synthesis of fat, accounts for the phenomena of the sparing action of fat on vitamin B. That is, if an animal is on a fat-free, vitamin B-free diet, the addition of fat supplies, perhaps, one essential that might also be supplied by vitamin B, and thus the animal is able to survive much longer on a vitamin B-free diet with fat than on the same diet without fat.

CONGENITAL DIABETES. DR. F. S. SMYTH, San Francisco.

The hereditary factor in diabetes has been repeatedly emphasized. These reports, however, are concerned with familial tendencies, not, strictly speaking, congenital diabetes. There is still considerable confusion regarding pregnancy in diabetes. At present it seems probable that under adequate control a diabetic woman may expect a fairly normal infant at the end of gestation.

Lawrence and others have emphasized the improvement in tolerance during gestation. Dubriel and Anderodias, and Gray and Funsten, have described instances of hyperplasia of the insular tissue in infants born of diabetic mothers, these infants also having symptoms of hypoglycemia. Since the appearance of these reports it has been customary in the University of California Hospital to consider the infants born of diabetic mothers as being particularly prone to hypoglycemia. Symptomatically, the infants show cyanotic spells and projectile vomiting suggestive of obstruction. The routine use of 3 per cent solution of dextrose given subcutaneously has proved of great value in these cases.

A follow-up of four of these patients showed that even at an older age the tolerance for dextrose is better than would be expected.

An infant who died with hypoglycemia shortly after birth was studied by complete pathologic examination. The macrosomia, advanced age and maturity of bone, increased thyroid colloid and persistent extramedullary hematopoiesis suggested a pituitary-like acceleration. This may be more than casual in the instances

in which control of the maternal diabetes is not adequate. Possibly insular hyperplasia with pituitary dysfunction is present, though the interrelation is not clear. After having investigated other reports of congenital diabetes, particularly those of Schretter and Nevinny, we are convinced that these authors are not dealing with diabetes but with hyperplasia of the islands of Langerhans associated with probable hyperfunction.

BASAL METABOLISM IN THE PERIOD OF GROWTH WITH RELATION TO THE PREVIOUS DIET. DR. J. A. JOHNSTON and DR. J. MARONEY, Detroit.

In 23 children ranging in age from 4 to 16 years kept on measured diets for periods averaging nine and one-fifth months, variations in the caloric and protein intakes were paralleled by spotted or continuous nitrogen balances and basal metabolic readings at regular intervals. The diets were started at submaintenance levels and increased to the point where there was growth and a positive nitrogen balance. The diets were then increased to maximum or superabundant levels. In some instances variations in the fat and carbohydrate content of the diets were made to determine the effect of these constituents on the basal heat production.

Definite lowering of the metabolism was evident constantly with submaintenance diets. While with increased intakes the basal heat production could in most subjects be brought from subnormal levels to normal, only slight increases beyond normal were evident, though such increases calculated on a basis of surface area were possible with high intakes of protein. The maximum elevation of the basal metabolism was a dual effect of calories and protein. The addition of a large increment of carbohydrate to an adequate diet was accompanied by a slight decrease in the basal heat production. Added increments of fat produced slight, and increments of protein marked, increases in the basal metabolism. The effects of the increased protein on the basal metabolism seem related to the amount of protein oxidized as opposed to the amount stored.

DISCUSSION

DR. D. C. DARROW, New Haven, Conn.: May I suggest that Dr. Du Bois be asked whether he wishes to comment on the paper?

DR. E. F. DU BOIS, New York: I have no comments to make on the first part of the paper, as it seems to me that the main points are brought out very well. If I am not mistaken, the greater specific dynamic action of metabolized protein and the absence of specific dynamic action of protein deposited were first demonstrated by Rubner. The specific dynamic action of protein is of clinical significance in fevers and accounts for some of the increase in total metabolism found in infectious diseases.

DR. S. Z. LEVINE, New York: I should like to ask Dr. Maroney whether he, in his ordinary control series of children on whom he does basal metabolism tests, gets fluctuations with the same technic approximating or anywhere nearly approaching the variations with changes in diet. I wondered whether Dr. Maroney did one, two or three measurements of the basal metabolism, and whether the reported figures represent averages or the results of single determinations.

DR. J. MARONEY, Detroit: Each of the points represents a single observation, but the children, as I said, were on these diets for an average of nine months each and were well trained subjects. In the control period there were three observations; they were identical.

ADDISONIAN PERNICIOUS ANEMIA IN INFANCY. DR. B. BENJAMIN, Brooklyn.

The history of two siblings is presented. The first, a boy, was admitted to the hospital in 1928 at the age of 2½ years. His birth and development were normal, and his diet was adequate. His illness began insidiously when he was about 21 months old, at which time his appetite failed and he began to vomit. Intermittent mild diarrhea gradually developed, and he became weak and was no longer able

to walk or stand. At 28 months he was found to have hyperchromic anemia. Hemoglobin was 34 per cent; erythrocytes numbered 1,410,000; there were leukopenia and an icteric index of 18.8. Although he received five transfusions over a period of four months, clinical improvement was only temporary, and he died of an intercurrent infection.

The second patient, a girl, was admitted to the hospital in 1933 at the age of 21 months. Her illness ran a course which her mother considered to be strikingly similar to that of the first child's illness. She developed normally until she was about 12 months old, at which time she began to vomit frequently. At 18 months she suffered from marked anorexia, was pale, apathetic and irritable and was no longer able to walk. Diarrhea was not present at any time. Examination revealed marked pallor and weakness, a barely palpable spleen and complete atrophy of the papillae of the tongue. The blood count showed hemoglobin, 30 per cent; erythrocytes, 1,370,000; leukocytes, 4,200; polymorphonuclears, 28 per cent; eosinophils, 1 per cent; lymphocytes, 67 per cent; mononuclears, 2 per cent; megaloblasts, 2 per cent, and normoblasts, 2 per cent. There were marked anisocytosis, poikilocytosis and polychromasia, with predominant macrocytosis. The mean corpuscular volume was 96 cubic microns; there were from 2 to 5 per cent reticulocytes, and from 40,000 to 70,000 platelets. The bleeding time was eight minutes; the icteric index was 10.3. Gastric analysis showed absence of free hydrochloric acid, and the urine showed increased excretion of urobilin. The fragility of the red blood corpuscles was normal.

In view of the great doubt regarding the existence of pernicious anemia in infancy, this diagnosis was not at first entertained, and an attempt was made to treat the patient by means of transfusions. Improvement resulting from this form of therapy was short-lived, however, the child becoming critically ill five weeks after the second transfusion. She was then given a parenteral injection of extract of 400 Gm. of liver, to which she responded promptly with a typical rise in reticulocytes followed by a complete clinical remission. No further treatment was administered, and the child remained well for several months, after which a relapse began, with the development of typical glossitis and a recurrence of the former symptoms. Injection of liver extract again resulted in a characteristic hematologic response. This sequence of events has been induced four times in two years, the duration of the period of remission varying according to the amount of liver extract employed.

Two months after the beginning of the first remission the patient still had achlorhydria. Several months later she was found to have recovered the ability to secrete free hydrochloric acid in the gastric juice. However, during the course of some tests carried out according to the method of Reimann for the presence of the gastric intrinsic factor it was observed that the oral administration of liver extract failed to bring about a remission.

DISCUSSION

DR. K. D. BLACKFAN, Boston: I think that in view of recent knowledge as to the criteria which are required for the diagnosis of pernicious anemia in adults one should adhere closely to those items in the pinning of the name "addisonian pernicious anemia" to anemia in children. As has been emphasized, there are several questionable features about this case. The presence of achlorhydria without response to histamine is not unusual even in macrocytic anemia, and, as one can note in this case, after two remissions there has been a return of the gastric acidity. It will be interesting to know the future progress of this feature.

With regard to the study of children with a condition diagnosed as pernicious anemia, it seems important to be sure that there is no interference with the absorbability of substances in the gastro-intestinal tract beyond, one might say, the stomach. In fact, I would place that as one item which perhaps one did not determine by a series of roentgenograms of the gastro-intestinal tract. With an

intestinal shunt or intestinal disease it is possible for a situation exactly comparable to the one presented here to develop.

As to the question of the return of hydrochloric acid in the stomach, I think that although it has been referred to as occurring occasionally in adults, it is not the rule. This is another point about which I would be careful before calling a condition specifically pernicious anemia as one recognizes it in adults.

Most of you who were here yesterday recall the discussion in regard to the paper presented by Dr. Klump as to the significance of the reticulocyte curves. From your chart I could not see how quickly the reticulocytes rose or how long it took them to return to normal. Also, there seems to be a sharp coincidental rise in hemoglobin and the red cells with the sharp rise in reticulocytes, whereas in the pernicious anemia of adults this rise is usually somewhat delayed.

In view of the great confusion which has existed in the literature regarding the diagnosis of pernicious anemia in children, as has been pointed out, before the days of the present conception of that disease, one should be quite sure of the diagnosis of pernicious anemia in children before such cases are reported in the literature.

Dr. B. Benjamin, Brooklyn: With regard to Dr. Blackfan's remarks, I should like to point out first that I do not think that an intestinal anomaly such as the one mentioned would explain the achlorhydria which was present early in the disease. On the other hand, Castle and others have reported that typical pernicious anemia in adults may be associated with faulty absorption from the intestinal tract, and that those patients respond only to liver given parenterally.

The reticulocyte response looked steep because the chart was much condensed and covered a period of several months. The beginning of the rise took place two days following the injection, reached its height on the sixth day and continued for eight days longer. In that respect it was entirely typical and was duplicated on a subsequent occasion.

I think that this answer applies also to the rise in hemoglobin and the red blood count.

Regarding the possibility that this may be a transitory condition, it seems hardly likely to me, since the condition has been present for three years and the patient has had several relapses when therapy was withheld.

A Case of Nontropical Sprue with a Blood Picture of Pernicious Anemia.

Dr. A. McBryde, Durham, N. C.

A child who had had symptoms characteristic of celiac disease since the age of 1 month, weighed 11 pounds (5 Kg.) at 27 months of age and had hyperchromic macrocytic anemia; the mean corpuscular volume was 148 cubic microns. Marked reticulocytosis occurred when bananas were added to the diet, and the blood picture approximated normal without the addition of iron or liver in any form. Two cases of sprue in adults are cited which show the exact picture seen in this case, with characteristic stools of high fat content, a hyperchromic blood picture, stomatitis, emaciation and weakness. Srue and celiac disease probably are one disease entity in persons of different age groups.

DISCUSSION

Dr. D. C. Darrow, New Haven, Conn.: I wonder whether the speaker was dealing with hyperchromic anemia in the same sense as pernicious anemia. I should think that one would have to demand response to the liver factor rather than something else to put this condition in exactly the same category as pernicious anemia. As I understand it, Rhodes has shown that the anemias that occur in sprue respond to liver in the same way as pernicious anemia does. I should also like to point out that in celiac disease, as contrasted with sprue, glossitis does not occur. It seems to me that while the evidence is very great that sprue and celiac disease are probably the same disease, children with celiac disease do not seem to show the disturbances which produce the pernicious anemia and glossitis in adults with sprue.

DR. A. MCBRYDE, Durham, N. C.: In reply to Dr. Darrow, I did not say that this child could not have had pernicious anemia. I do not think that it is due to the absence of the same factor. I think that if anything was missing it probably was the so-called extrinsic factor. In fact, our observations on the reticulocyte count seem to show that it has little to do with the other factor. We had no type of food that would contain the extrinsic factor.

I forgot to mention that when this child was 17 months of age she had pertussis, glossitis and stomatitis. Whether one should call this case one of infantile sprue which is not celiac disease I do not know. In many cases of sprue one finds that the hydrochloric acid in the stomach is perfectly normal, and in these three cases in adults the hydrochloric acid was perfectly normal.

Book Reviews

Emotions and Bodily Changes: A Survey of Literature on Psychosomatic Interrelationships, 1910-1933. By H. Flanders Dunbar. Price, $5. Pp. 595. New York: Columbia University Press, 1935.

The avowed purpose of this volume is that of furnishing a discriminative review of the vast literature pertinent to the subject which has accumulated in nearly a quarter of a century. The ample cross-section of this literature which is offered is indicated by a bibliography of more than twenty-two hundred titles. Nor is this important feature of the book distinguished only by its length. It represents a prudent culling from a much larger body of writings, and one gains the conviction that the examples selected include both the most important and the most characteristic contributions to this field. So the bibliography alone forms an extremely useful working instrument for any one interested in this particularly active aspect of contemporary medicine.

The work is arranged into a general section devoted largely to contributions from biologists, anatomists, physiologists, psychologists, psychoanalysts and clinicians on the development of the concept of the total organism in health and disease. This includes an instructive chapter dealing with various physical methods of measurement which have been used extensively to detect the play of psychic factors in the economy of the organism, such as psychogalvanometry and quantitative biochemical and biophysical observations. This is followed by a larger section in which disturbed functions and the structure of the separate organ systems are considered in their relationships to psychic energy, more particularly to the affective components of the psyche. A short discussion of therapeutic considerations follows.

While the work purports to be a digest of data, of views and of theories, it is in reality more than this. By his selection and arrangement of material, Dunbar has achieved the elaboration of a thesis, a thesis neatly put in his quotation from Mohr: "There is no such thing as a purely psychic illness or a purely physical one, but only a living event taking place in a living organism which is itself alive only by virtue of the fact that in it psychic and somatic are united in a unity." It is the author's method to let the material recorded speak for itself, but now and again he interjects his own criticism, which is always sound and often trenchant. Throughout there is a definite bias, so to speak, toward psychoanalytic doctrine, especially from the therapeutic angle. Regardless of the merits or demerits of psychoanalysis, the reason for this is plain. While a realization of the potency of the psyche in all illness is voiced from many sides by orthodox clinicians, it is the discipline of psychoanalysis almost alone which attempts to lend precision and meaning to such terms as nervousness and emotion. Here only are there a real collecting of facts and the striving for a rationale. This is a book which may be read with profit by all physicians in all fields. It should be a useful corrective for many a specialist who fails to see the woods for his preoccupation with his own particular tree.

The Diseases of Children. Edited by Dr. M. von Pfaundler and Dr. A. Schlossmann. English translation by M. G. Peterman, Sc.B., A.M., M.D., American editor-in-chief, with the cooperation of 21 American pediatricians. Five volumes. Pp. 544; 512; 689; 575; 546, with 76 full-page plates and 1,129 illustrations. Price, $45. Philadelphia: J. B. Lippincott Company, 1935.

This is the English translation of the fourth edition of this standard German pediatric system. The first volume deals with a history of pediatrics, the biology of development, morbidity and mortality in childhood, child welfare and the examination of children, with a consideration of childhood pharmacotherapy, in the first

two hundred pages. The last three hundred pages are devoted to the physiology of nutrition, diseases of the new-born and premature infant, the physiology of puberty and poisonings in childhood. The second volume contains a discussion of constitutional diseases, deficiency diseases, diseases of the blood, endocrine glands and diseases of the circulatory system. The third volume is concerned with the infectious diseases, rheumatic fever, syphilis and tuberculosis. The fourth volume deals with diseases of the respiratory system and diseases of the digestive system, with a discussion of nutrition. The fifth volume treats of the diseases of the genito-urinary system, diseases of the nervous system and diseases of the motor apparatus.

To those readers who are familiar with the older editions, while the same general scheme of treatment of the various subjects has been carried out, there has been a complete revision of contents. All authors who were not able to revise their sections were replaced. Göppert, Niemann, Pirquet and Salge have been removed by death. The following are now co-authors: Beumer, Bischoff, Bossert, Degkwitz, Freudenberg, Goebel, György, Hottinger, Keller, Leichtentritt, Lust, Moro, Nitschke, Opitz, von Reuss, Rott, de Rudder, Hans Schlossmann, Stoeltzner, Stolte and Vogt. An entire new section has been added on tropical diseases in children by Bisdom of Java.

As to the general text, enough can hardly be said. The descriptions are excellent and completely cover all points that the student might desire. The illustrations are beautiful and bring out all the necessary points. Peterman has added many from his own collection to supplement those of the original book. The translation has been well done, and the editor deserves much credit for his work. The edition is well bound, and the printing and paper are excellent. In brief, this edition will be found to be of great interest to the student, as well as to the practicing pediatrician.

Food for the Young Child. By Miriam E. Lowenberg. Price, $1.50. Pp. 142, with 5 illustrations. Ames, Iowa: The Collegiate Press, Inc., 1934.

This is an unusual and valuable book on food for young children. As its basis is scientifically sound and its presentation practical, it is particularly good for the mother, the teacher, the nutrition worker and the physician. In fact, any one interested in raising "the standards for foods to be fed to children" will find it helpful.

In addition to supplying a large number of menus and recipes, the book covers the problem of child feeding in a more general way. The suggestions for the planning of menus and the preparation and serving of food would indicate that the author has successfully fed large numbers of children and is able to speak authoritatively.

The general plan for feeding children is conservative and well rounded. There are no foods that are emphasized to the exclusion of others, and there is a general recognition that, when necessary, it is possible to substitute one food for another. For example, while the author believes that it is practically impossible to furnish an adequate diet for the growing child that does not contain some milk, she sees the disadvantage of forcing milk under certain conditions and suggests that fruit juice may be substituted for milk for a period even as long as two weeks.

She believes that few foods are unsuitable for small children, but suggests that it is safer to eliminate questionable foods than to take a chance on them. She explains why color, texture and flavor of the food are important. Practical suggestions, such as the child's meal being fitted into the adult's meal to reduce extra work for the mother, are given. The importance of proper meal service in comfortable and attractive surroundings is stressed.

In the chapter entitled "Eating" the author emphasizes the importance of good food habits and makes many suggestions for developing these, such as the establishing of the right emotional state for eating by avoiding emotional outbreaks preceding a meal.

The menus are very attractive and most complete for the main meal of the day—dinner. A number of typical menus for breakfast and supper are added, which should be helpful for those planning the three meals. The recipes are appropriate and well worked out. On the whole, this is a book which will be gratefully accepted by those interested in feeding children.

Theory and Practice of Anaesthesia. By M. D. Nosworthy, M.A., M.D., B.Ch. (Cantab.), Anaesthetist to Westminster Hospital, Anaesthetist to Grosvenor Hospital for Women, Late Senior Resident Anaesthetist, St. Thomas's Hospital. With a foreword by L. W. Magill, M.D., B.Ch. (Belf.), Senior Anaesthetist to Westminster Hospital, Anaesthetist to Brompton Hospital for Consumption and Diseases of the Chest. Price, 12 shillings, sixpence. Pp. 223, with 35 illustrations. London: Messrs. Hutchinson & Co., 1935.

This volume is divided into sixteen chapters and covers the subject of anesthetics and anesthesia completely, though not exhaustively. The text is clearly written from an evident background of wide experience. The book is well organized, each subject being discussed in individual chapters. A bibliography appended to each chapter simplifies references to the subject.

Because of its brevity, this volume will commend itself more as a reference work for anesthetists than as a textbook for undergraduates. The author wisely states: "It is a mistake to force any anaesthetic beyond the point which marks the safety line with that particular agent."

In spite of the fact that the dangers of chloroform are recognized and discussed, Nosworthy suggests its employment alone or combined with nitrous oxide. American anesthetists almost without exception believe that ether is as efficient and infinitely safer than chloroform. The author's faith in carbon dioxide as a cure-all for undesirable conditions during and following anesthesia is noticeable throughout the book.

King, in a controlled series, reported the results of his study which showed that routine postoperative inhalation of carbon dioxide was of no greater value in the prevention of postoperative pulmonary complications than a frequent change of position.

Methodik der Vitaminforschung. By Christian Bomskov, D.Ph. Price, paper, 24 marks; bound, 26 marks. Pp. 301, with 92 illustrations and 109 tables. Leipzig: Georg Thieme, 1935.

This excellent book is intended for the use of any one who may wish to employ animals in research on vitamins. It is an extremely minute, inclusive and up-to-date summary of the technics used in producing various types of hypovitaminosis and hypervitaminosis and in the concentration, purification and assay of vitamin preparations. The illustrations include photographs of suggested animal cages, roentgenograms of characteristic bone lesions, typical weight curves and pictures of animals manifesting various hypovitaminotic symptoms. There are many tables which should be useful in making up diets. The bibliography shows an appreciation of American work that is not always seen in the European literature. The table of contents and index are complete. Other and larger compendiums of information on vitamins have been written, but none, so far as is known to us, is so devoted to the needs of the laboratory worker or so specific in its directions for special procedures. A copy of it should be in the library of any institution which teaches physiology or biochemistry or which maintains facilities for nutritional research.

L'année pédiatrique. By Robert Broca and Julien Marie. Price, 25 francs. Pp. 168, with 46 illustrations. Paris: Masson et Cie, 1934.

There is no attempt in this volume to cover the whole field of pediatrics. The authors have chosen for discussion clinical conditions which have recently been recognized or concerning which there has been significant recent progress. They

are both clinicians of note and present their subjects with great understanding. The illustrations are excellent.

The chapter headings are: (1) Acrodynia, (2) Still's Disease, (3) Malignant Lymphogranulomatosis (Hodgkin's Disease), (4) Meningococcemia, (5) Lipoid Nephrosis in the Child, (6) Pyocephaly of the Infant, (7) Subacute Curable Pulmonary Edema of the Infant, (8) Dried Milk Fever, (9) The Rôle of Vitamins in Infancy, (10) Ulcer of Meckel's Diverticulum, (11) Acute Ethmoiditis in the Infant, (12) Anterior Tibial Apophysitis, (13) Primary Acute and Subacute Orchitis of Infancy, (14) The Treatment of Colon Bacillus Pyelonephritis, (15) Recent Progress in Antidiphtheritic Vaccination, (16) Modern Methods of Measles Prophylaxis and (17) The Roentgenography of the Lung in Erythema Nodosum.

Infantile Paralysis. By George Draper, M.D. Price, $2. Pp. 167, with 24 illustrations. New York: D. Appleton-Century Company, Inc., 1935.

Draper has accomplished the task that he set for himself in producing a book on infantile paralysis which is both "readable and intelligible." Only a vast experience over many years and an extensive, intimate knowledge of the progress of the work could make possible so concise and simple an exposition.

For the layman the subject is presented in a fashion that makes it comprehensible, removing most of the mysterious aspects. More than that, the book presents this disease so that it is not so terrifying and offers hope both before and after the disease is encountered.

Despite its simplicity this book is really of untold value to the physician. It presents the medical aspects of the disease in a clearcut fashion, and the chapters on diagnosis and the discussion of treatment are very thorough. In addition, it summarizes the progress of investigation in a clear and orderly fashion, pointing out the unsolved features that still exist and indicating the direction in which further research may lead to a solution of these problems.

One Thousand Questions and Answers on T. B. Edited by Fred H. Heise, M.D., medical director, Trudeau Sanatorium. Cloth. Price, 75 cents. Pp. 232. New York: Journal of Outdoor Life, 1935.

These questions and answers have been selected from about four thousand which have come to question-box of the *Journal of Outdoor Life* during the past ten years. This book is intended for the education of the adult or adolescent tuberculous patient. Heise aims to supplement but not to replace the advice of the attending physician. In the main, he has succeeded. In a few instances, discrepancies must have occurred, but the author is particularly careful to recognize his limitations in giving advice in absentia and insists on consultation with the physician in the settlement of many of the questions. He also admits freely the limitations of present knowledge in certain directions. A note of justifiable optimism obtains throughout, without engendering a false sense of security.

The New-Born Baby. By Eric Pritchard, M.A., M.D., F.R.C.P. Cloth. Price, 4 shillings, sixpence. Pp. 284, with 9 figures. London: Henry Kimpton, 1934.

This book consists of a series of lectures which Pritchard has given to students on the subject of the care of new-born babies. It is divided into twenty-five chapters covering clothing, management of the child, feeding, disturbances of feeding, premature infants and the common diseases existing in the new-born.

The book is interesting reading for any one wishing to review the subject. It has the common failing of books of this size: It is too complicated for mothers who wish information and not detailed enough for any one wishing to specialize in the subject. It is even too complicated for the class of persons for whom it was evidently written—midwives and maternity nurses. However, it is an interesting book for the pediatrician who wishes to find out the manner in which the new-born baby is cared for in England.

Physiology in Modern Medicine. By J. J. R. MacLeod. Seventh edition. Price, $8.50. Pp. 1154, with 297 illustrations. St. Louis: C. V. Mosby Company, 1935.

This excellent text is now in its seventh edition. This edition has among its authors Philip Bard, M.D., Johns Hopkins University; Edward P. Carter, M.D., John's Hopkins University; J. M. D. Olmstead, M.D., University of California; J. M. Peterson, M.D., University of Aberdeen, and N. B. Taylor, M.D., University of Toronto.

Many of the chapters have been rewritten, and the whole book has been brought up to date. It is especially full in consideration of the physiology of the circulatory system, but the whole volume is such as to appeal to one interested in scientific medicine. It should prove a boon to students and practitioners, who will find few texts which contain this information.

Illustrative Electrocardiography. By Joseph H. Bainton and Julius Burstein. Price, $5. Pp. 258, with 100 illustrations. New York: D. Appleton-Century Company, Inc., 1935.

The major part of this monograph is a practical demonstration of the various abnormalities which occur in the electrocardiogram. Chapters 1 and 2 deal with fundamentals and normal variations. The illustrations are clearly marked and analyzed. No theoretical considerations are attempted and no clinical data given except in the chapter on "T Wave Abnormalities and Coronary Thrombosis." This is a very simplified text and contains the essentials for analysis of an electrocardiogram.

Directory of Pediatric Societies *

INTERNATIONAL

International Association of Preventive Pediatrics

President: Professor G. Scheltema, 6a Heereplein, Groningen, The Netherlands.
Secretary: Dr. Daniel Oltramare, 15 Rue Lévrier, Geneva, Switzerland.

FOREIGN

British Paediatric Association

President: Dr. Hugh Thursfield, 84, Wimpole St., London, W. 1.
Secretary: Dr. Arthur G. Maitland Jones, 31 A, Weymouth St., London, W. 1.

Royal Society of Medicine, Section for the Study of Disease in Children

President: Sir Lancelot Barrington-Ward, 85 Harley St., London, W. 1.
Secretary: Dr. K. H. Tallerman, 122 Harley St., London, W. 1.
Place: 1, Wimpole St., London. Time: Fourth Friday of each month, 4:30 p. m.

Paediatrický Spolok na Slovensku

President: Dr. A. J. Chura, Lazaretská 6, Bratislava, Czechoslovakia.
Secretary: Dr. S. Limbacher, Dlhá 2, Bratislava, Czechoslovakia.
Place: Pediatric Clinic, University, Bratislava. Time: Six times a year.

NATIONAL

American Medical Association, Scientific Assembly, Section on Diseases of Children

Chairman: Dr. Horton R. Casparis, Vanderbilt University Hospital, Nashville, Tenn.
Secretary: Dr. Ralph M. Tyson, 255 S. 17th St., Philadelphia.
Place: Kansas City, Mo. Time: May 11-15, 1936.

American Academy of Pediatrics

President: Dr. Henry Dietrich, 1136 W. Sixth St., Los Angeles.
Secretary: Dr. C. G. Grulee, 636 Church St., Evanston, Ill.
Region I. Place: Boston. Time: Fall, 1936.
Regions II and III. Place: Hotel Chase, St. Louis. Time: Nov. 18-19, 1935.
Region IV. Place and time not yet decided.

American Child Health Association

President: Dr. Samuel McC. Hamill, 1822 Spruce St., Philadelphia.
Secretary: Dr. Philip Van Ingen, 125 E. 71st St., New York.

American Hospital Association, Children's Hospital Section

President: Mr. Robert Witham, Children's Hospital, Denver.
Secretary: Miss Agnes O'Roke, Kosair Crippled Children's Hospital, Louisville, Ky.

American Pediatric Society

President: Dr. Fritz B. Talbot, 270 Commonwealth Ave., Boston.
Secretary-Treasurer: Dr. Hugh McCulloch, 325 N. Euclid St., St. Louis.

* Secretaries of societies are requested to furnish the information necessary to make this list complete and to keep it up to date.

CANADIAN SOCIETY FOR THE STUDY OF DISEASES OF CHILDREN

President: Dr. A. P. Hart, 1844 Bloor St., W., Toronto, Ont.
Secretary-Treasurer: Dr. Pearl Summerfeldt, Hospital for Sick Children, Toronto, Ont.

SOCIETY FOR PEDIATRIC RESEARCH

President: Dr. C. F. McKhann, Children's Hospital, Boston.
Secretary: Dr. A. A. Weech, 3975 Broadway, New York.

SECTIONAL

NORTH PACIFIC PEDIATRIC SOCIETY

President: Dr. L. Howard Smith, 1020 S. W. Taylor St., Portland, Ore.
Secretary: Dr. Morris Bridgeman, Children's Clinic, Portland, Ore.

SOUTHERN MEDICAL ASSOCIATION, SECTION ON PEDIATRICS

Chairman: Dr. Luther W. Holloway, 117 W. Duval St., Jacksonville, Fla.
Secretary: Dr. Madison Hines Roberts, 104 Ponce de Leon Ave., N. E., Atlanta, Ga.
Place: St. Louis. Time: Nov. 19-22, 1935.

STATE

ALABAMA PEDIATRIC SOCIETY

President: Dr. J. W. Britton, 931 Noble St., Anniston.
Secretary-Treasurer: Dr. Wallace Clyde, Employees' Hospital, Fairfield.

ARKANSAS STATE PEDIATRIC ASSOCIATION

Chairman: Dr. Morgan Smith, 625 Beech St., Little Rock.
Secretary: Dr. Madeline A. M. Melson, 2111 N. Spruce St., Little Rock.

CALIFORNIA STATE MEDICAL SOCIETY, SECTION ON PEDIATRICS

Chairman: Dr. S. J. McClendon, 2001 Fourth Ave., San Diego.
Secretary: Dr. Edward B. Shaw, 384 Post St., San Francisco.
Place: Coronado. Time: May 25-28, 1936.

GEORGIA PEDIATRIC SOCIETY

President: Dr. William Willis Anderson, 478 Peachtree St., Atlanta.
Secretary-Treasurer: Dr. Roger W. Dickson, 33 Ponce de Leon Ave., N. E., Atlanta.
Place: Atlanta, December 1935. Savannah, June 1936.

INDIANA STATE PEDIATRIC SOCIETY

President: Dr. Louis H. Segar, 23 E. Ohio St., Indianapolis.
Secretary-Treasurer: Dr. Mathew Winters, 23 E. Ohio St., Indianapolis.
Time: Two meetings a year.

LOUISIANA STATE PEDIATRIC SOCIETY

President: Dr. Charles James Bloom, 3439 Prytania St., New Orleans.
Secretary-Treasurer: Dr. J. A. Crawford, 834 Ryan St., Lake Charles.

MEDICAL SOCIETY OF STATE OF NEW YORK, SECTION ON PEDIATRICS

Chairman: Dr. George M. Retan, 459 James St., Syracuse.
Secretary: Dr. John D. Craig, 33 E. 61st St., New York.
Place: New York City. Time: April 27-29, 1936.

MICHIGAN STATE MEDICAL SOCIETY, PEDIATRIC SECTION

Chairman: Dr. Edgar E. Martmer, 749 David Whitney Bldg., Detroit.
Secretary: Dr. C. R. Dengler, 131 W. Michigan Ave., Jackson.

MISSISSIPPI STATE PEDIATRIC SOCIETY

President: Dr. R. E. Wilson, 205 S. Harvey St., Greenville.
Secretary-Treasurer: Dr. Guy C. Jarratt, 920 Crawford St., Vicksburg.
Place: To be designated by Society. Time: Yearly.

NEBRASKA PEDIATRIC SOCIETY

President: Dr. J. A. Henske, 1614 Medical Arts Bldg., Omaha.
Secretary-Treasurer: Dr. J. H. Murphy, 915 Medical Arts Bldg., Omaha.
Place: As announced by committee. Time: Third Thursday of each month from October to June, inclusive. Dinner at 6 p. m.

NORTH CAROLINA PEDIATRIC SOCIETY

President: Dr. J. R. Ashe, 306 N. Tryon St., Charlotte.
Secretary: Dr. R. A. Moore, 306 N. Tryon St., Charlotte.
Place: Pinehurst. Time: May 6, 1936.

OKLAHOMA STATE PEDIATRIC SOCIETY

President: Dr. Julian Feild, 610 S. Monroe St., Enid.
Secretary: Dr. B. H. Nicholson, 301 N. W. Twelfth St., Oklahoma City.

PENNSYLVANIA MEDICAL SOCIETY, PEDIATRIC SECTION

Chairman: Dr. Francis T. O'Donnell, 345 North Main St., Wilkes-Barre.
Secretary: Dr. Theodore O. Elterich, 119 S. Highland Ave., Pittsburgh.

SOUTH CAROLINA PEDIATRIC SOCIETY

President: Dr. William Weston Jr., 1428 Lady St., Columbia.
Secretary-Treasurer: Dr. Leland B. Salters, 317 S. Warley Ave., Florence.

TENNESSEE STATE PEDIATRIC SOCIETY

President: Dr. Joe T. Smith, 702 Medical Arts Bldg., Knoxville.
Secretary: Dr. Kinsey M. Buck, 1193 Madison Ave., Memphis.
Place: Memphis. Time: April 1936.

TEXAS PEDIATRIC SOCIETY

President: Dr. C. O. Terrell, 813 Medical Arts Bldg., Fort Worth.
Secretary-Treasurer: Dr. F. H. Lancaster, 1507 Medical Arts Bldg., Houston.

VIRGINIA PEDIATRIC SOCIETY

President: Dr. Basil B. Jones, 1028 W. Franklin St., Richmond.
Secretary: Dr. W. A. McGee, 616 W. Grace St., Richmond.

WEST VIRGINIA STATE MEDICAL SOCIETY, SECTION ON PEDIATRICS

President: Dr. John T. Thornton, 58, 16th St., Wheeling.
Secretary: Dr. Claude L. Holland, 400 Locust Ave., Fairmont.

LOCAL

ACADEMY OF MEDICINE OF CLEVELAND, PEDIATRIC SECTION

Chairman: Dr. J. D. Pilcher, City Hospital, Cleveland.
Secretary: Dr. William M. Champion, 2323 Prospect Ave., Cleveland.
Place: Cleveland Medical Library Bldg. Time: October, December, February and April.

ACADEMY OF MEDICINE, TORONTO, SECTION OF PEDIATRICS

President: Dr. T. B. Verner, 170 St. George St., Toronto.
Secretary: Dr. D. V. Hutton, 170 St. George St., Toronto.

Bronx Pediatric Society

President: Dr. Harry M. Shapiro, 1882 Grand Concourse, New York.
Secretary: Dr. Daniel J. Dolan, 420 E. 159th St., New York.
Place: Concourse Plaza Hotel, 161st St. and Grand Concourse. Time: Every second Wednesday of each month, except June, July, August and September.

Brooklyn Academy of Pediatrics

President: Dr. W. F. Watton, 240 Berkeley Pl., Brooklyn.
Secretary: John A. Monfort, 861 Carroll St., Brooklyn.
Place: Kings County Medical Society Bldg. Time: Fourth Wednesday of each month, except May, June, July, August and September.

Central New York Pediatric Club

President: Dr. Frank Vander Bogert, 111 Union St., Schenectady.
Secretary: Dr. Frank J. Williams, 58 S. Swan St., Albany.
Place: Various cities in New York. Time: Third Thursday of April and September.

Chicago Pediatric Society

President: Dr. A. Levinson, 30 N. Michigan Ave., Chicago.
Secretary: Dr. James H. Wallace, 715 Lake St., Oak Park, Ill.
Place: Children's Memorial Hospital, 710 Fullerton Ave. Time: Third Tuesday of each month.

Dallas County Pediatric Society

President: Dr. P. E. Luecke, 4105 Live Oak St., Dallas, Texas.
Secretary: Dr. R. S. Usry, 1835 Garrett Ave., Dallas, Texas.
Place: Bradford Memorial Hospital. Time: 1 p. m., first and third Saturdays of each month.

Detroit Pediatric Society

President: Dr. Edgar E. Martmer, 749 David Whitney Bldg., Detroit.
Secretary: Dr. W. J. Scott, 5140 Second Ave., Detroit.
Place: Wayne County Medical Society. Time: 8:30 p. m., first Wednesday of each month.

Fulton County Medical Society, Pediatric Section (Atlanta, Ga.)

Chairman: Dr. Joseph Yampolsky, 478 Peachtree St., Atlanta.
Secretary: Dr. T. I. Willingham, 384 Peachtree St., Atlanta.
Place: Academy of Medicine, 38 Prescott St., N. E. Time: Second Thursday of each month from October to April, 8 p. m.

Harris County Pediatric Society

President: Dr. Byron P. York, 3820 Fannin St., Houston, Texas.
Secretary-Treasurer: Dr. E. O. Fitch, 3717 Main St., Houston, Texas.
Place: Houston Club. Time: Third Monday of each month.

Intermountain Pediatric Society

President: Dr. Helmina Jeidell, 11 Exchange Pl., Salt Lake City, Utah.
Secretary-Treasurer: Dr. Edwin R. Murphy, 9 Exchange Pl., Salt Lake City, Utah.
Place: Salt Lake City, General Hospital. Time: First Thursday of each month, 8 p. m.

Kansas City (Missouri) Pediatric Society

President: Dr. Harry M. Gilkey, 1103 Grand Ave., Kansas City.
Secretary: Dr. S. A. Stadler, 6133 Brookside Blvd., Kansas City.
Place: Kansas City General Hospital. Time: On call.

MEDICAL SOCIETY OF THE COUNTY OF KINGS AND THE ACADEMY OF MEDICINE OF BROOKLYN, PEDIATRIC SECTION

President: Dr. Charles F. Fisher, 756 Eastern Parkway, Brooklyn.
Secretary: Dr. Harry Apfel, 988 Park Pl., Brooklyn.
Place: 1313 Bedford Ave., Brooklyn. Time: Third Wednesday of each month, October to May.

MEDICAL SOCIETY OF THE COUNTY OF QUEENS, INC., SECTION ON PEDIATRICS

Chairman: Dr. Henry A. Reisman, 148, 88th Ave., Jamaica, L. I.
Secretary-Treasurer: Dr. Edith A. Mittell, 112 Queens Blvd., Forest Hills, N. Y.
Place: Queens County Medical Bldg., Forest Hills, N. Y. Time: Third Monday of October, January, March and May.

MEMPHIS PEDIATRIC SOCIETY

President: Dr. W. D. Mims, 1042 Madison Ave., Memphis, Tenn.
Secretary-Treasurer: Dr. W. R. Graves, 1193 Madison Ave., Memphis, Tenn.
Place: Memphis General Hospital. Time: Second Tuesday of each month, except June, July and August, 8 p. m.

MILWAUKEE PEDIATRIC SOCIETY

President: Dr. J. Gurney Taylor, 324 E. Wisconsin St., Milwaukee.
Secretary: Dr. H. B. Miner, 425 E. Wisconsin Ave., Milwaukee.
Place: Children's Hospital. Time: Second Wednesday of each alternate month, beginning with February.

NEW ENGLAND PEDIATRIC SOCIETY

President: Dr. Paul Emerson, 319 Longwood Ave., Boston.
Secretary-Treasurer: Dr. Henry E. Gallup, 66 Commonwealth Ave., Boston.
Place: Boston Medical Library. Time: Four meetings a year, occurring from September to May.

NEW YORK ACADEMY OF MEDICINE, SECTION OF PEDIATRICS

Chairman: Dr. Béla Schick, 17 E. 84th St., New York.
Secretary: Dr. Alexander T. Martin, 107 E. 85th St., New York.
Place: New York Academy of Medicine, 2 E. 103d St. Time: Second Thursday of each month from October to May, inclusive, 8:30 p. m.

NORTHWESTERN PEDIATRIC SOCIETY

President: Dr. E. F. Robb, 1801 Lyndale Ave., S., Minneapolis.
Secretary: Dr. A. V. Stoesser, University Hospital, Minneapolis.

PHILADELPHIA PEDIATRIC SOCIETY

President: Dr. John D. Donnelly, 115 Bryn Mawr Ave., Bala, Pa.
Secretary: Dr. James E. Bowman, 4091 Comly St., Philadelphia.
Place: College of Physicians, 19 S. 22d St. Time: Second Tuesday of each month from October to June, inclusive.

PITTSBURGH PEDIATRIC SOCIETY

President: Dr. George J. Feldstein, 3401 5th Ave., Pittsburgh.
Secretary-Treasurer: Dr. E. R. McClusky, 3200 Fifth Ave., Pittsburgh.
Place: Pittsburgh Academy of Medicine. Time: Second Tuesday, alternate months from October to April, inclusive.

RICHMOND PEDIATRIC SOCIETY

President: Dr. Samuel A. Anderson Jr., 2326 W. Grace St., Richmond, Va.
Secretary-Treasurer: Dr. Emily Gardner, 1100 W. Franklin St., Richmond, Va.
Place: Richmond Academy of Medicine, 1200 E. Clay St. Time: First Thursday of each month (except July, August and September).

ROCHESTER PEDIATRIC SOCIETY

President: Dr. F. W. Bush, 29 N. Goodman St., Rochester, N. Y.
Secretary: Dr. David Wolin, 16 N. Goodman St., Rochester, N. Y.
Place: Arranged by program committee. Time: Second Friday of each month.

ROCKY MOUNTAIN PEDIATRIC SOCIETY

President: Dr. Ralph Verploeg, 1850 Gilpin St., Denver.
Secretary: Dr. Max M. Ginsburg, Metropolitan Bldg., Denver.
Place: Children's Hospital, Denver. Time: First Saturday of each month from September to May, inclusive, 2:30 p. m.

ST. LOUIS PEDIATRIC SOCIETY

President: Dr. J. V. Cooke, St. Louis Children's Hospital, St. Louis.
Secretary-Treasurer: Dr. Katherine Bain, Beaumont Bldg., St. Louis.
Place: St. Louis Medical Society. Time: Third Friday of every month.

SEATTLE PEDIATRIC SOCIETY

President: Dr. Arthur E. Wade, 1215, 4th Ave., Seattle.
Secretary: Dr. Walter B. Seelye, Cobb Bldg., Seattle.
Place: College Club. Time: Third Friday of each month, 6:30 p. m.

SOUTHWESTERN PEDIATRIC SOCIETY

President: Dr. Victor E. Stork, 1136 W. Sixth St., Los Angeles.
Secretary: Dr. Howard R. Cooder, 3875 Wilshire Blvd., Los Angeles.
Place: University Club of Los Angeles. Time: First Wednesday in January, March, May, September and November.

UNIVERSITY OF MICHIGAN PEDIATRIC AND INFECTIOUS DISEASE SOCIETY

President: Dr. Daniel Budson, 3001 W. Grand Blvd., Detroit.
Secretary: Dr. D. Murray Cowie, University of Michigan, Ann Arbor, Mich.
Place: Ann Arbor, Mich. Time: Nov. 22-23, 1935.

WESTCHESTER COUNTY MEDICAL SOCIETY, PEDIATRIC SECTION (NEW YORK)

President: Dr. Louis V. Waldron, 149 N. Broadway, Yonkers, N. Y.
Secretary-Treasurer: Dr. Fairfax Hall, 421 Huguenot St., New Rochelle, N. Y.
Place: Grasslands Hospital. Time: Third Thursday, Oct., Dec., Feb. and April.

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